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ELECTROKYMOGRAPHIC STUDIES OF THE LEFT AURICULAR MOVEMENTS IN MITRAL STENOSIS AND INSUFFICIENCY

by

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Changes appear in the electrokymograms from the auricles as well as from the ventricles and the great vessels in cases of mitral valve disease. Such observations have been described in the literature by numerous writers (KJELLBERG & RUDHE; LUISADA & FLEISCHNER; LUISADA, ROMANO & TORRE; BOONE, RANDAK, ELLINGER & OPPENHEIMER; LIAN, FAQUET & MINOT; MC KINNON & FRIEDMANN; MARSHAL; ANDERSSON). The majority of the changes observed are in the electrokymogram of the left auricle, caused by the regurgitation in insufficiency, and changes in the electrokymogram of the left ventricle. In addition, KJELLBERG & RUDHE described how the part of the auricular curve depending upon the contraction is accentuated in mitral stenosis. The same phenomenon was mentioned by the author. LUISADA & FLEISCHNER noted that a similar accentuation can occur in hypertrophy of the left auricle.

Only changes in the electrokymogram of the left auricle are discussed in detail in the present paper, which is a preliminary report of a more extensive investigation. The behavior of the other chambers of the heart and the great vessels will be treated only to the extent of its essential significance in the understanding of the electrokymogram of the left auricle. The report is based upon a material of 90 cases of mitral valve disease with sinus rhythm with which it principally deals.

For information concerning the electrokymographic apparatus and the methods of examination, the reader is referred to the special articles which have appeared (KJELLBERG & RUDHE; BOONE & HENNY; LUI-

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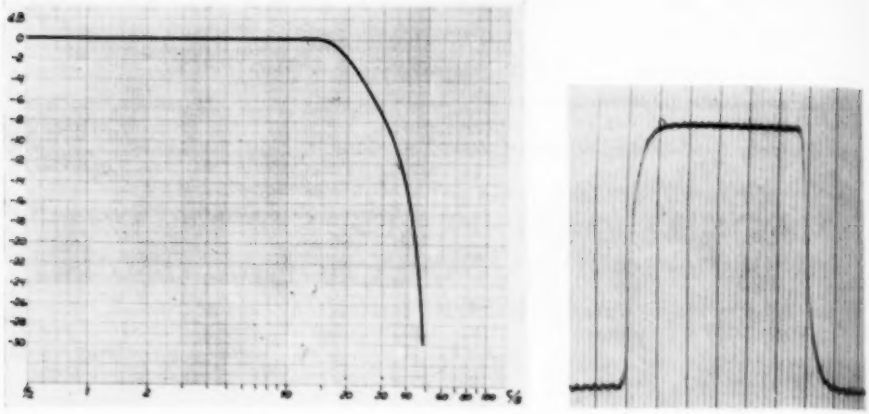


a. b.

Fig. 1 a. Frequency curve of the electrokymograph used.
b. Square impulse reproduced by the same apparatus.

SADA & FLEISCHNER; MORGAN; LIAN & MINOT; MARSHAL). The apparatus used in this investigation is in principle of the same construction as the one described by the author in a previous paper. However, some alterations in the amplifying and filter systems have been made. Certain technical data must therefore be mentioned. (In a small number of the cases the original apparatus was used.)

In order to determine the accuracy with which the electrokymographic curves reproduce the movements of the cardiac contour, it is necessary to know which frequencies the apparatus used can reproduce and which are suppressed. Figure 1 shows a frequency curve from the apparatus used by the writer. It is apparent from the curve that frequencies up to 15—20 cycles per second are reproduced practically unattenuated, while higher frequencies are reproduced with diminishing amplitude. From 50 cycles per second upwards, all impulses are cut-off by filters in order to eliminate the 50 and 100 cycle disturbances from the high tension system and the roentgen apparatus. These filters produce a certain distortion of the curves as may be seen from figure 1 b, which shows how the apparatus reproduces a square impulse. The beginning of the impulse is correctly reproduced, but its termination is somewhat deformed.

A rising characteristic in the electrokymographic curves reproduced indicates an outward movement of the cardiac contour while a fall represents an inward movement.

An electrokymographic curve is, in the main, an expression of the movements of the cardiac contour at a certain point or over a small area. This movement is composed of different components dependent upon changes in volume, movements transmitted between the chambers of the heart and movements of the heart as a whole. (Movements of the latter type may be called positional changes.) The recording of different types of movements on the same curve gives the electrokymogram a complicated appearance; not least, in the case of the curves from the auricles, which have movements influenced to a great extent by those of the ventricles and the great arteries. Furthermore, the movements of the auricles are subjected to wide variations; *e. g.* by changes in the intrathoracic pressure and varying body positions.

Before the pathologic curves in mitral valve disease are discussed, the electrokymogram of the normal auricle will be described.

On the normal auricular electrokymogram (figures 2 and 3), there is a falling curve, depending upon a decrease in volume, principally during auricular systole and the period of rapid inflow during early diastole. A rising curve, depending upon an increase in volume, is observed corresponding to the later part of ventricular diastole during the period of reduced inflow and to the later part of ventricular systole, during the period of reduced ejection.

In the transitional periods between systole and diastole, falls and rises in the curve occur owing to positional changes.

In figure 2, somewhat idealized auricular curves in relation to electrocardiograms and carotid pulse curves are presented schematically. The phases of the cardiac cycle are denoted according to WIGGERS. Figure 3 shows typical auricular electrokymograms from normal patients.

It is evident from the curves reproduced, that in auricular systole, after the P wave of the electrocardiogram, the course is downward for a short distance, due to the contraction of the auricle (beginning approximately 0.12 of a second after P).

Subsequently, there is a short horizontal portion followed by small rise (usually beginning 0.02 to 0.04 of a second after the R wave). This rise is due to the isometric contraction of the ventricle. The curve changes when ejection begins (about 0.10 of a second after the R wave) to a falling course of somewhat varying duration. This movement occurs because the auricles passively follow the ventricular systolic contraction primarily owing to the large movement of the atrioventricular septum towards the apex.

In the examination in the upright position the curves have a mainly horizontal or very gradually rising characteristic during the later part of the ejection. Thus, according to the electrokymogram only a slight

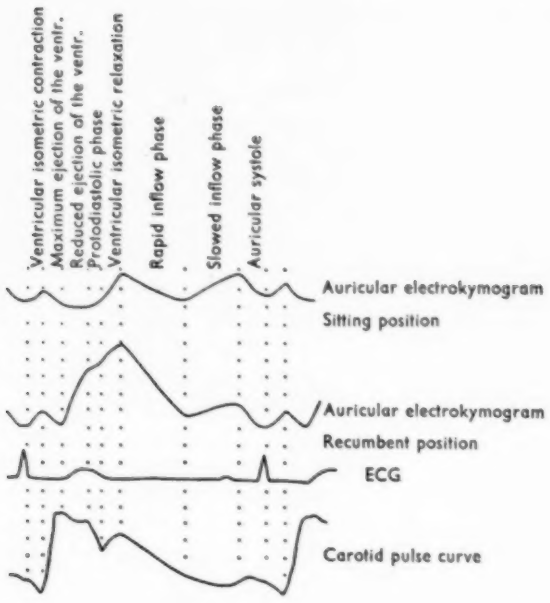


Fig. 2.

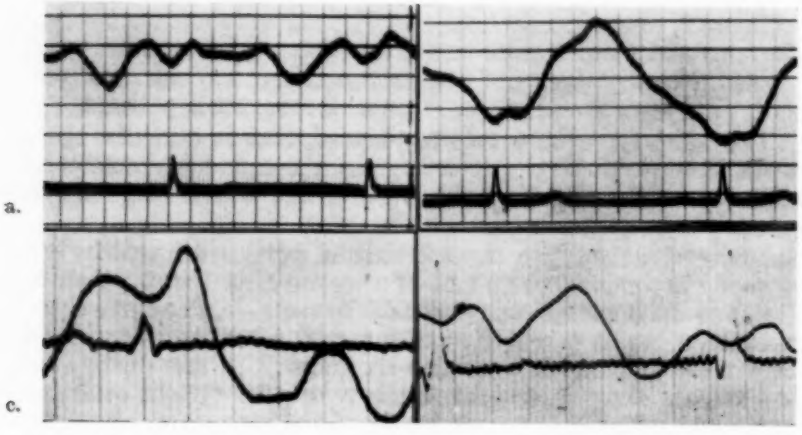


Fig. 3. Auricular electrokymograms from normal subjects. a and b are recorded in the same region of the right auricle in a healthy person in the sitting and recumbent positions respectively. c and d are normal variations of auricular curves recorded in the sitting position.

increase, or none at all, in the auricular volume should occur in the erect posture during the period in question.

Corresponding to the last part of the T wave, the curve generally rises steeply during a few hundredth parts of a second. This rise depends upon a positional change during the isometric relaxation period.

When the atrioventricular valves are opened, blood flows from the auricles to the ventricles, decreasing the volume of the former. Therefore, the curve falls rather sharply during the rapid inflow period. During the slowed inflow period, the auricular curves generally more or less rise. Accordingly, the auricular volume usually increases during this part of diastole. However, it seems as if the rise during the reduced inflow period might be partially due to transmitted movement from the ventricle, especially in the case of higher cardiac frequency.

The curve type described is valid when the examination is made with the patient in the upright position (the upper curve in fig. 2 and figs. 3 a, c, and d). However some difference exists between the curves in the upright and recumbent position. In the recumbent position the curves generally rise during the last part of the ventricular systole, the period of reduced ejection (Fig. 2 lower curve and fig. 3 b).

The curve fall after the atrioventricular valves are opened is generally correspondingly greater in the recumbent position. The variation in the curve in the upright and recumbent positions may be explained by the differing haemodynamic conditions.

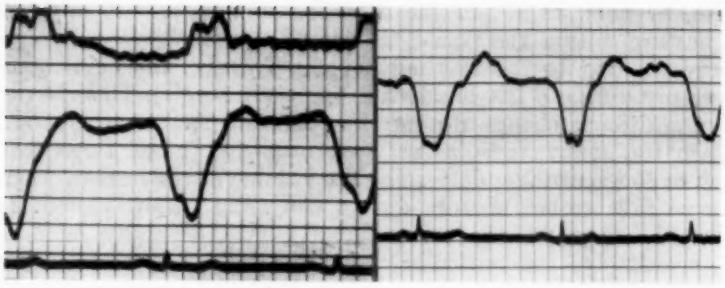
Should the auricular curve rise during the last part of the ventricular systole, it then generally changes to a more horizontal course corresponding to protodiastole. During the following isometric relaxation it rises again, as mentioned above. These are positional changes.

The time relations of the electrokymogram are fairly constant during systole, regardless of the frequency; on the other hand, this is not true during diastole. This depends upon the well known fact that changes in the cardiac frequency within moderate limits affect primarily the duration of diastole, while the systolic period is less affected.

As mentioned earlier, auricular electrokymograms to a certain extent have a varying appearance. The time relationships and the direction of movement are but little affected by the variations although the relation between the magnitude of the different movement factors may vary.

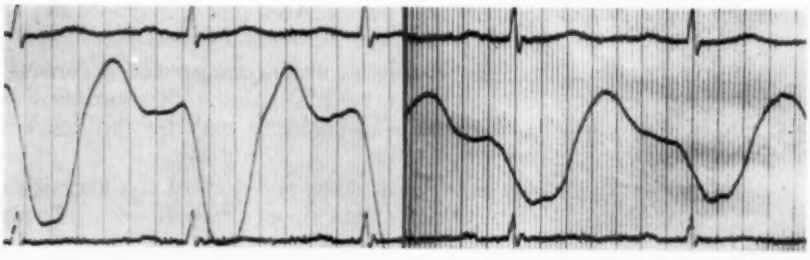
The movements of the auricular appendices are sometimes differentiated from those of the auricles through a stronger contraction, but the direction and time relations are the same.

Concerning variations due to frequency, it must be mentioned that the auricular contraction is relatively small at low and greater at high frequency. In the case of tachycardia, the curve after the opening of



a. b.

Fig. 4 a. Curve from the left auricular appendix in a patient with mitral stenosis. Note the large auriculosystolic movement, the plateau-like appearance and the steep rise during the last part of ventricular systole. b is recorded in the posterior part of the left auricle in the same patient. The two curves are practically identical. (The upper curve in a is a carotid pulse tracing.)

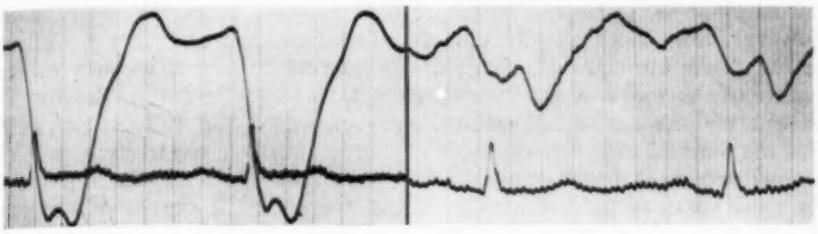


c. d.

Fig. 4 c and d are curves from the left auricular appendix and the posterior part of the left auricle in a patient with mitral stenosis. The auricular appendix curve c shows pronounced pathologic changes (compare fig. 4 a and b), while the changes, *e. g.* the auricular contraction, are less in d.

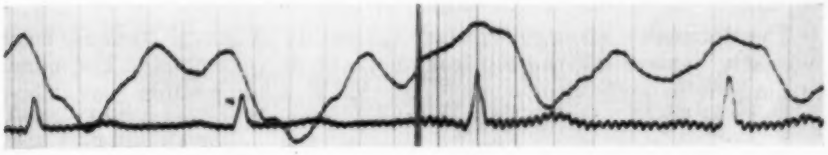
the atrioventricular valves, due to the short diastolic period, appears to pass directly into the auricular contraction.

In mitral valve disease, the most pronounced and typical changes are observed in the curves of the left auricle. Stenosis and insufficiency each present characteristic curves. In most cases, they appear simultaneously. However, not infrequently, one component appears unmixed or is dominant. In the present material, curves with only signs of stenosis comprise a greater number of cases than curves with only signs of insufficiency. (This is true in the case of sinus rhythm, but when auricular fibrillation appears, mitral stenosis presents no characteristic changes



e. f.

Fig. 4 e and f are corresponding curves from another case of mitral stenosis. In this case the difference between the auricular appendix curve, e, and the curve of the posterior part of the left auricle, f, is still more pronounced.



g. h.

Fig. 4 g and h. Mitral stenosis. The curve of the left auricular appendix, g, shows typical pathologic changes, while the curve of the posterior part of the left auricle in the same patient, h, has a normal appearance.

in the auricular curve, while insufficiency reveals itself to the same extent as with sinus rhythm.)

The most striking and characteristic electrokymographic change in mitral stenosis is an accentuation of the falling portion of the left auricular curves, which is dependent upon the auricular contraction. The accentuation is in most cases of high degree. It includes both the amplitude and duration of the contraction wave (figure 4).

Another change may be seen earlier in diastole when the auricle is in the passive phase. The curve falls less then than normally, after the mitral valves are opened, and the curve frequently assumes a plateau-like appearance.

Both of the changes described depend upon the reduced flow through the narrow ostium with a damming up of blood in the auricle and a strengthened auricular contraction.

Finally, the curve rises more abruptly than normally during the later part of ventricular systole, probably because of increased pulmonary venous pressure (figure 4).

The curve type described in the foregoing paragraphs, constituting a graphic presentation of the movements of the left auricular wall in

mitral stenosis, is characteristic of that disease. It is worthy of note, however, that these movements of the wall are not completely uniform in the entire auricle. Just as there are anatomic differences between the nature of the wall in the auricular appendix and in the rest of the auricle, there are also some variations in the movements of the wall. Accordingly, the movements represented by the aforementioned electrokymographic curves are most conspicuous in the region of the auricular appendix. In some cases of unquestionable mitral stenosis, the curves of the posterior part of the auricle show no definitely pathologic movements (figure 4 h), but typical pathologic electrokymograms are obtained of the auricular appendix (figure 4 g). In other cases, however, the curves of the different parts of the auricle are practically identical (figures 4 a and b), while in most cases, the pathologic features are less marked in the auricle itself than in the auricular appendix (figures 4 c—f).

The noticeably strong auricular contraction in mitral stenosis, made so clearly evident by the electrokymogram, is remarkable. The mitral ostium is narrowed, often severely, so that it is improbable that a large quantity of blood, corresponding to the decrease in volume of the auricle during contraction, will be forced into the left ventricle during a brief period. (The electrokymogram affords no direct measure of volumetric change, but if it registers a simultaneous centripetal or centrifugal movement of the wall in all parts of a chamber of the heart, a corresponding change in the volume of the chamber must take place.) Sometimes a more abrupt rise during presystole, corresponding to a more rapid filling, may be observed in the ventricular curves; it is however never extensive and there is usually but a slight rise or none at all. The probable explanation is that a large part of the decrease in volume of the left auricle at the time of the contraction takes place through forced reflux of the blood into the pulmonary veins. Frequently, postcardial curves show a rise during auricular systole, probably caused by veins dilated in this manner.

A few cases illustrate the electrokymographic observations in mitral stenosis:

Case 1, S. D., a man, aged 48; history of scarlatina and typhus fever but not of rheumatic disease. He was admitted to the medical department for long-standing abdominal discomfort, headache and pains in the cardiac region. Auscultation of the heart revealed an abrupt and accentuated first sound at the apex; no blowing murmur. Roentgenologic examination disclosed moderate enlargement of the left auricle. An electrokymographic examination resulted in typical mitral stenosis curves from the left auricle (figure 5).

A few days after the examination, the patient contracted pulmonary oedema and died. A postmortem examination revealed a postendocarditic mitral stenosis in which the ostium admitted only the tip of a little finger.

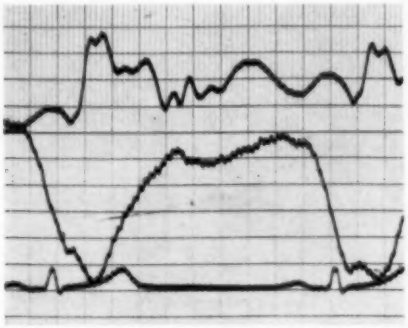


Fig. 5. Case 1. Electrokymogram of the left auricular appendix. Compare fig. 4.

Case 2, G. N. Cardiac disease was discovered in this woman, aged 42, in connection with clinical and electrokymographic examinations undertaken for the purpose of assembling a normal material. However, the patient had long had shortness of breath. Auscultation of the heart revealed blowing sounds typical of mitral stenosis. Roentgenologic examination showed enlargement of the left auricle.

The results of the electrokymographic examination were as follows:

Examination I) Sinus rhythm, and left auricular curves typical of mitral stenosis were observed (figure 6 a). (Examination II, approximately 5 months after examination I.) Auricular fibrillation had appeared. The strongly falling characteristic of the curve, representing the auricular contraction observed in examination I, had entirely disappeared. The curve had a horizontal course during presystole (figure 6 b).

Case 3, H. A., a woman, aged 42, had long had recognized mitral stenosis. Clinical examination and catheterization were typical of mitral stenosis. Roentgenologic examination revealed enlargement of the left auricle. The preoperative electrokymographic examination showed curves from the left auricle with typical mitral stenosis course (figure 7 a). Commissurotomy was performed by Professor Crafoord.

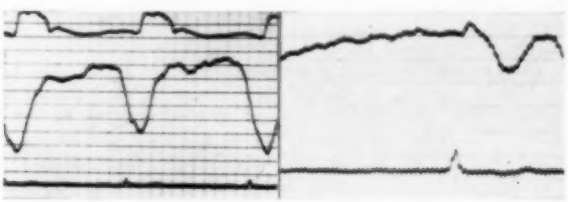


Fig. 6. Case 2. Electrokymograms recorded in the left auricular appendix region; mitral stenosis. a. with sinus rhythm (examination I). Note the typical changes with the large auriculosystolic movement. b. after auricular fibrillation had appeared (examination II). The marked auriculosystolic movement has disappeared. The curve has a horizontal course during presystole.

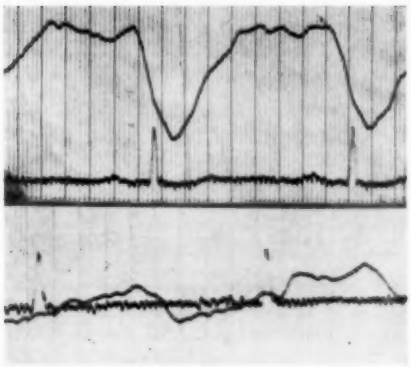


Fig. 7. Case 3. Electrokymograms from the left auricle; mitral stenosis. a, recorded before operation, shows the typical signs of mitral stenosis. In b, recorded after operation, the signs of stenosis have disappeared.

The postoperative electrokymographic examination demonstrated that the curves from the left auricle had attained a normal course (figure 7 b) (*i. e.*, concerning the stenosis component, the postoperative curves from the auricle exhibit a certain insufficiency, which is in agreement with the postoperative catheterization findings).

Cases 2 and 3 illustrate how the strongly falling characteristic of the curves in presystole is dependent upon the auricular contraction. In case 2, this disappears in the auricular curve when the rhythm changes to auricular fibrillation. In case 3, the contraction after the stenosis has been relieved by operation has the same appearance as in normal cases.

Case 4, E. N., a girl aged 13, had exhibited signs of cardiac disease since early childhood; *i. e.*, shortness of breath and palpitation of the heart. Auscultation revealed a weak systolic blowing sound. A distant presystolic blowing sound was heard after exercise. A roentgenologic examination showed marked bulging at the site of the left auricular appendix. The right ventricle appeared enlarged. An angiocardiographic examination revealed that the left auricle was spherical and larger than normal. Catheterization showed no indications of shunts within the heart or in the great vessels. The oxygen saturation in the pulmonary artery was 70 per cent by volume. The pressure in the pulmonary artery was 60/26 mm Hg, PCV 24 to 25 mm Hg. There were no indications of insufficiency in the PCV curve.

An electrokymographic examination showed the auricular systolic wave to be stronger than normally in the curves from the left auricular appendix although not to such a great extent as in the curves reproduced in figures 4 and 5 a, 6 a and 7 a. This was the only deviation from the normal (figure 8).

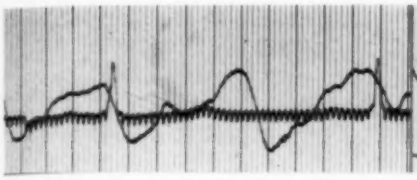


Fig. 8. Case 4. Left auricular appendix curve. The auriculosystolic movement is moderately accentuated.

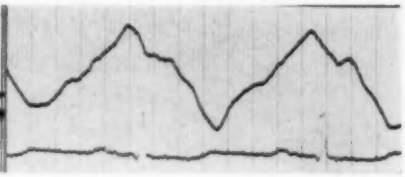


Fig. 9. Case 5. Curve from the left auricular appendix. No pathologic signs.

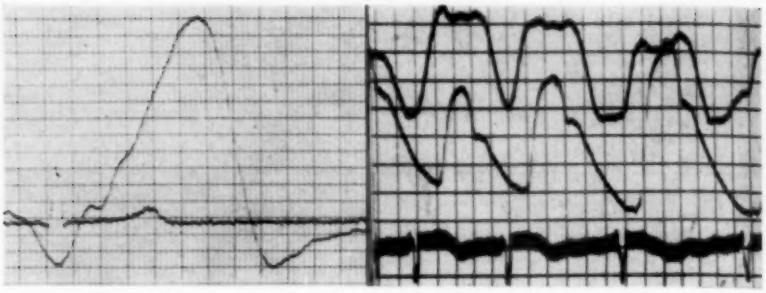
This was an example of mitral stenosis in a very young person. It was probably congenital. The electrokymographic examination disclosed only a moderate accentuation of the contraction wave in the curves from the left auricular appendix. It is obvious that the stenosis must reach a certain severity before the pronounced electrokymographic changes described earlier can appear. In cases with relatively little stenosis, the electrokymograms may show only slight deviations from the normal.

Case 5, T. E., a woman aged 49, had had recognized heart disease for about 25 years. She complained of shortness of breath and swelling of the lower limbs. Conspicuous cyanosis was observed. Auscultation revealed a presystolic blowing sound. A roentgenologic examination showed the right ventricle to be enlarged and the left auricle to be moderately enlarged. No bulging of the left auricular appendix was observed. The pulmonary artery and its branches were extensively dilatated — more than is usual in mitral stenosis. Angiocardiograms showed the left auricle to be moderately enlarged. There was no filling of the left auricular appendix with contrast medium. Catheterization showed the pressure in the pulmonary artery to be 79—92 cm/H_2O.

The electrokymograms of the left auricle showed no characteristic changes, except an early slight rise during systole in the curves from the posterior parts indicating a certain insufficiency. The auricular contraction was of ordinary magnitude (figure 9).

Operation (digital valvulotomy) was performed by Professor Crafoord. The left auricle did not appear very large. The auricular appendix was small — the size of a thumb's end. The ostium was of hardly a pencil's width. During operation the pressure in the left auricle was recorded by a cannula inserted through a pulmonary vein. The intra-auricular pressure curve showed only little rise during the auricular contraction.

The cause of the atypical electrokymogram in this case (which is in agreement with the intra-auricular pressure curve recorded during operation) is not clear. The pulmonary arterial hypertension recorded at the catheterization (and during the operation as well) may be of importance in this connection. If pathologic changes of the arteries cause obstruction of the blood flow in the pulmonary circulation the left auricle is, so to speak, unloaded. In such cases typical mitral stenosis curves can probably not be expected. Moreover, the fact that the left auricular appendix



a. b.

Fig. 10 a and b. Left auricular electrokymograms from patients with mitral insufficiency. The curves rise during the ventricular systole including the isometric contraction period. The short falls of the curves corresponding to the introduction of the ventricular systolic ejection are clearly visible. (The middle curve in b is a carotid pulse tracing.)

c. d.

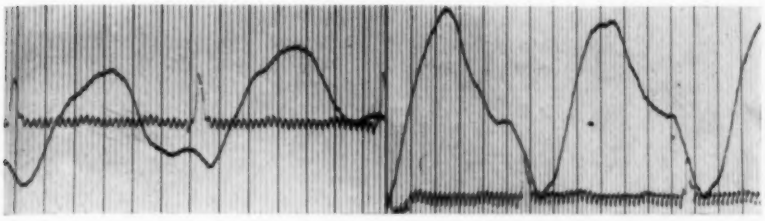
Fig. 10 c and d. Left auricular electrokymograms from patients with mitral insufficiency. The curves rise during the ventricular systole.

was very small must be taken into consideration as in many cases typical curves are obtained only from that part of the auricle.

In insufficiency of the mitral ostium, blood is forced back into the left auricle during the contraction of the left ventricle, thereby effecting a dilatation of the auricle. This appears as a rise in the electrokymographic curves of the left auricle.

As described earlier, the auricular curve normally falls during the first (the maximum) period of the ventricular ejection.

In mitral insufficiency, the auricular curve rises steeply during the entire ventricular systole, owing to the expansion of the auricle (figure 10). The rise also takes place during the isometric contraction. Thus, the auricle is already dilated during that period.



a. b.

Fig. 11. Case 6. Electrokymograms of the left auricular appendix, a, and the posterior part of the left auricle, b. Compare figs. 4 and 10.

The curve rises most during the isometric contraction and the beginning of the ejection, being subsequently rounded off during the later part of this phase. The rise generally continues until the time of the opening of the mitral valves in normal hearts, *i. e.* the beginning of the period of rapid inflow, after which the curve falls. In certain cases, however, the curve reaches its maximum earlier — in the beginning of the period of maximum ejection (figure 10 b). The insufficiency in these cases, is probably of such a high degree that the auricle becomes maximally dilated early. During the later part of systole, in these cases, the curve mostly runs horizontally and forms a plateau.

Hence, it is evident that the auricular curve in mitral insufficiency rises during the whole of systole. This rise is generally interrupted, however, at the transition between the isometric contraction and the ejection periods. As in normal patients, the ventricle, particularly the atrioventricular septum, causes a centripetal coincident movement in the auricular wall during the first part of the ejection. This is expressed in the curve of the left auricle as a falling characteristic. In mitral insufficiency, however, this is small and shorter than normally. Immediately after this short fall, the curve rises again (figures 10 a and d).

The point where the auricular slope changes from a rise to a fall corresponds to the introduction of the ejection in normal persons and also in cases in which there is stenosis but no insufficiency. This is apparent from a comparison with the aorta-electrokymogram or the carotid pulse curve. In many cases of severe mitral insufficiency, however, the curve changes a few hundredths of a second later. This is probably caused by the regurgitation, which more and less compensates for the coincident movement in the auricular wall (figure 10 b). In the present material, this downward course of the curve begins about 0.12 of a second after the beginning of the QRS complex in the »pure stenosis curves». In patients with severe insufficiency, corresponding movement

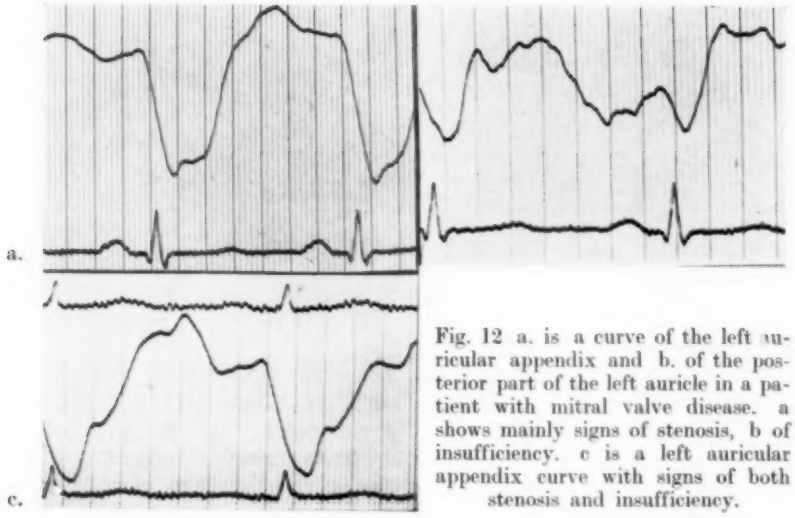


Fig. 12 a. is a curve of the left auricular appendix and b. of the posterior part of the left auricle in a patient with mitral valve disease. a shows mainly signs of stenosis, b of insufficiency. c is a left auricular appendix curve with signs of both stenosis and insufficiency.

occurs approximately 0.16 to 0.18 of a second after the beginning of the QRS complex.

As is the case with stenosis, the conditions in insufficiency are somewhat different in the auricular appendix and the auricle itself. Thus, the signs of insufficiency are more prominent in the electrokymogram in the latter than in the former. In certain cases, the curves from the left auricular appendix show slight or no signs of insufficiency, but the curves from the posterior parts of the auricle rise strongly during ventricular systole (figures 12 a and b).

In this connection, one condition is worthy of note. In the case of varying heart frequency, such as auricular fibrillation and extra-systole, the electrokymograms might show differences in the movements of the auricular wall with slow and rapid rhythm. If the auricular curve has a typical appearance of insufficiency in slow rhythm, the condition is the same when the rhythm is rapid. However, in cases where the auricular curves in slow rhythm do not approximate to this form, it is still possible that in rapid rhythm the auricle will exhibit movements similar to those seen in insufficiency. This occurs after particularly short diastoles and can appear in curves from both auricles. It can occur even if the cause of the arrhythmia is other than valvular disease, for example in cardiosclerosis. The phenomenon seems to occur at a lower frequency in cases of pure mitral stenosis than with auricular fibrillation of other genesis. The insufficiency represented by these electrokymographic

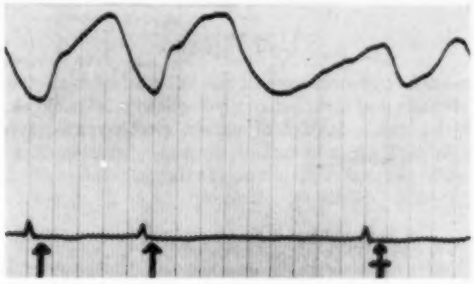


Fig. 13. Auricular curve in a patient with mitral stenosis and auricular fibrillation. After a short diastole there are signs of insufficiency (→), but not after a longer diastole (- ➤).

changes is probably of functional origin. After a very short diastole, the valves, chordae tendineae and papillary muscles are in an unfavourable position to hinder regurgitation when the early systole occurs, thus resulting in functional insufficiency (figure 13). This electrokymographic observation is in agreement with findings at cardio-catheterization that indicate insufficiency of the aforementioned type in the same cases. The writer has not observed any similar functional insufficiency, in sinus rhythm with tachycardia.

The following case illustrates the electrokymographic changes in insufficiency:

Case 6, A. L., a man, aged 30, had rheumatic polyarthritis in 1943. Heart disease was found in 1951. Auscultation revealed diastolic and systolic blowing sounds. Roentgenologic examination showed the left auricle to be enlarged. Catheterization (Hansson, Malmström) indicated predominating mitral insufficiency with stenosis to a lesser degree.

Electrokymographic curves of the left auricle rose during ventricular systole. The auricular contraction in the curves of the auricular appendix was greater than normal. The contraction wave, however, was only moderately increased (figure 11).

The electrokymographic changes described in stenosis and insufficiency of the mitral ostium occur in combination more frequently than alone. In the present material, isolated stenosis is more common than isolated insufficiency. In the great majority of cases, however, both conditions occurred simultaneously, frequently with one predominating in the electrokymogram (figure 7 c). Pure insufficiency appeared in only a few cases.

SUMMARY

A report is presented of the changes in the left auricular electrokymogram in mitral valve disease. Both stenosis and insufficiency present typical electrokymographic changes. These are illustrated by cases, in one of which, electrokymographic examination was performed both before and after operation (mitral stenosis). The article in the main deals with conditions associated with sinus rhythm.

ZUSAMMENFASSUNG

Es wird ein Bericht über Veränderungen des Elektrokymogrammes des linken Vorhofes bei Mitralisvitien gegeben. Sowohl die Stenose als auch die Insuffizienz geben typische elektrokymographische Veränderungen. Diese werden durch einige Fälle illustriert. In einem von diesen wurde Elektrokymographie sowohl vor als nach der Operation (Mitralisstenose) ausgeführt. Der Bericht umfasst hauptsächlich die Verhältnisse bei Sinusrythmus.

RÉSUMÉ

L'auteur décrit les modifications de l'électrokymogramme de l'oreillette gauche dans les affections mitrales; le rétrécissement et l'insuffiance donnent lieu à des modifications typiques; illustrées par quelques exemples. Dans l'un des cas présentés des électrokymogrammes ont été faits avant et après l'opération (rétrécissement mitral).

REFERENCES

1. Andersson, T.: A design for an electrokymograph and some fundamental considerations on the electrokymogram. Acta Radiol. 32 (1949), 276.
2. Andersson, T.: Electrokymographic recording of auricular movements. Acta radiol. 32 (1949), 121.
3. Boone, B. R., Chamberlain, W. E., Gillick, F. G., Henny, G. C. & Oppenheimer, M. J.: Interpreting the electrokymogram of heart and great vessel motion. Am. Heart J. 34 (1947), 560.
4. Coblenz, B., Harvey, R. M., Ferrer, M. J., Cournand, A. & Richards, D. W.: The relationships between electrical and mechanical events in the cardiac cycle of man. Brit. Heart J. 11 (1949), 1.
5. Engström, B., Kjellberg, S. R., Persson, L. & Rudhe, U.: Some aspects of the use of electrokymography in cardiac investigation. Acta radiol. 32 (1949), 435.
6. Henny, G. C. & Boone, B. R.: Electrokymograph for recording heart motion utilizing the roentgenoscope. Am. J. Roentgenol. 54 (1945), 217.
7. Henny, G. C. & Boone, B. R.: Improved electrokymograph for recording heart motion. Am. J. Roentgenol. 57 (1945), 409.
8. Lagerlöf, H., Holmgren, A. & Werkö, L.: Tidsrelationerna mellan hjärtats elektriska, mekaniska och akustiska impulser hos människa. (Swedish.) Nord. med. 3 (1949), 1422.
9. Lagerlöf, H. & Werkö, L.: The pulmonary capillary venous pressure pulse in man. Scandinav. J. Clin. & Lab. Invest. 1 (1949), 147.
10. Lian, C. & Minot, G.: La radioélectrokymographie. Arch. d. mal. du cœur. 39 (1946), 339.

11. Lian, C., Faquet, J. & Minot, G.: La radioélectrokymographie. Interprétation des courbes physiologiques. Application au problème des cardiopathies valvulaires mitrales. Arch. d. mal. du cœur. 41 (1948), 727.
12. Luisada, A. A., & Fleischner, F. G.: Dynamics of the left auricle in mitral valve lesions. Am. J. Med. 4 (1948), 791.
13. Luisada, A. A. & Fleischner, F. G.: Simultaneous fluorocardiography and recording of intracardiac pressure. Proc. Soc. Exper. Biol. & Med. 70 (1949), 730.
14. Luisada, A. A., Fleischner, F. G. & Rappaport, M. B.: Fluorocardiography (electrokymography). I. Am. Heart J. 35 (1948), 336. II. Am. Heart J. 35 (1948), 348.
15. Luisada, A. A., Romano, F. J. & Torre, I. M.: Isometric relaxation period of the left ventricle in normal subjects and patients with mitral stenosis. Proc. Soc. Exper. Biol. & Med. 69 (1948), 23.
16. McKinnon, J. B. & Friedman, B.: Electrokymographic studies of the left atrium in normal and diseased hearts. Circulation 2 (1950), 572.
17. Morgan, R. H.: Review: Electrokymography. Am. J. M. Sc. 218 (1948), 791.
18. Soulié, P., Di Matteo, J. & Marshal, M.: La cinédensigraphie dans l'insuffisance tricuspidienne. L'expansion auriculaire. La fois systolique. Arch. d. mal du cœur. 44 (1951), 1.
19. Wiggers, C. J.: Physiology in health and disease. Philadelphia 1945.

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MICROANGIOGRAPHY

by

S. Bellman and *A. Engström*

Microradiography has proved to be of value in a variety of research fields. In biology especially microradiographic methods have given new information about the chemistry and physics of cells and tissues that could hardly be obtained with other methods (for survey see ENGSTRÖM 1950).

In 1942—1944 BOHATYRTSCHUK applied the technique of microradiography to the study of the capillaries in biological tissues. The blood vessels were made roentgen opaque by the injection of a suitable contrast. A Bucky roentgen tube was used as source of radiation. The field of microarteriography was further developed by BARCLAY and his associates in England. The pictures published by BARCLAY are of a very high quality (the posthumous monograph covering BARCLAY's work forms a general reference).

When the blood vessel system is injected with a suitable roentgen contrast the capillaries and veins and not only the arteries, are filled. We therefore suggest 'microangiography' as a general term for the procedure.

Theoretical Aspects

Figure 1 shows a schematic cross-section of tissue with a blood vessel containing roentgen contrast. The roentgen ray absorption in the tissue may be expressed in the following way:

$$I_1 = I_0 \cdot e^{-\mu_1 \cdot t_1} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad 1\,a$$

where μ_1 is the linear absorption coefficient (cm^{-1}) and t_1 the thickness of the sample in cm. Generally, the mass absorption coefficient $\frac{\mu}{\varrho}$ ($cm^2\,g^{-1}$) is used and equation 1 a may be written,

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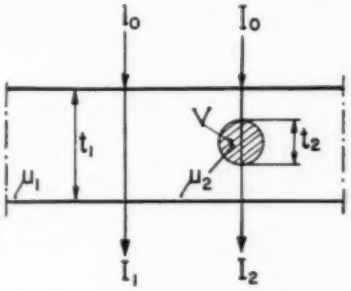

Figure 1. Schematic cross-section of tissue of thickness t_1 containing a contrast filled blood vessel, V, of thickness t_2. I_0 is the intensity of the incident and I_1 and I_2 of the transmitted roentgen rays. μ_1 and μ_2 are the linear absorption coefficients for the soft tissue and the contrast in the vessel.

$$I_1 = I_0 \cdot e^{-\frac{\mu_1}{\varrho_1} \cdot q_1} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad 1\,b$$

where q is the weight per unit area of the sample (g cm^{-2}). The roentgen rays passing through the tissue and the blood vessel with the thickness t_2 and linear absorption coefficient μ_2 are absorbed according to the following expression

$$I_2 = I_0 \cdot e^{-[\mu_1 \cdot (t_1 - t_2) + \mu_2 \cdot t_2]} \quad \ldots\ldots\ldots\ldots\ldots \quad 2$$

Combining equations 1 a and 2 we obtain

$$\frac{I_2}{I_1} = e^{t_2 \cdot (\mu_1 - \mu_2)} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad 3$$

The blackening, D, of a photographic emulsion is *in a certain range* (see below) proportional to the roentgen ray exposure,

$$D = \text{const.} \cdot I \cdot h \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad 4$$

where h is the time and I the intensity of the roentgen rays. Equation 3 may therefore be written (MÜLLER):

$$^{e}\log \frac{D_2}{D_1} = t_2 (\mu_1 - \mu_2) \ldots\ldots\ldots\ldots\ldots\ldots \quad 5$$

When evaluating the possible biological applications of microangiography the equations derived above are used to estimate the roentgen transmission of the objects. For such calculations the mass absorption coefficients must be known. Figure 2 shows the mass absorption coefficients as function of wavelength for different elements of interest in connection with this investigation. The linear absorption coefficient is obtained by multiplying the values in the diagram with the specific gravity of the element or substance in question. The transmission through various thicknesses of soft tissue layers for different wavelengths (cf. ENGSTRÖM 1946) is shown in figure 3. The soft tissue is simply assumed to have a density of 1, *i. e.* to be wet. Most soft tissues contain 70—80 % water. For exact calculations this assumption is not valid but it

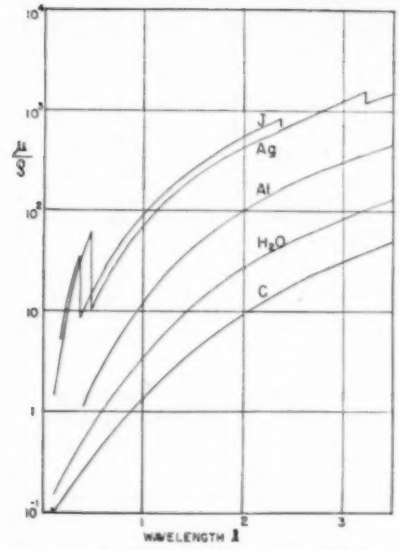

Figure 2. Mass absorption coefficients for certain elements of interest in micro-angiography.

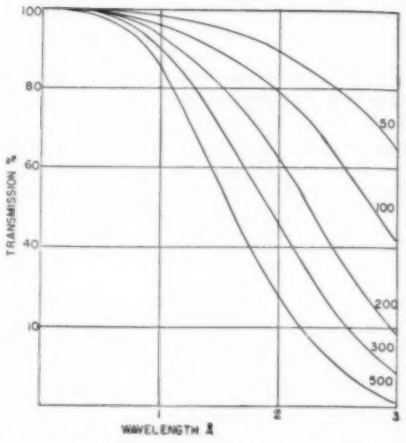

Figure 3. The transmission of roentgen rays in various thicknesses of a soft tissue, *e. g.* kidney, for different wavelengths. The figures on the curves give the thickness in microns.

gives enough accuracy in the present evaluation. From figure 3 it can be seen that a slice of soft tissue 0.5 mm thick, *e. g.* a section of a kidney, has an absorption of about 13 % at 1 Å wavelength. Thus if high absorption is required from the tissue soft and ultrasoft roentgen rays have to be used. On the other hand, if little absorption is desired roentgen rays with wavelengths shorter than 1 Å may be used.

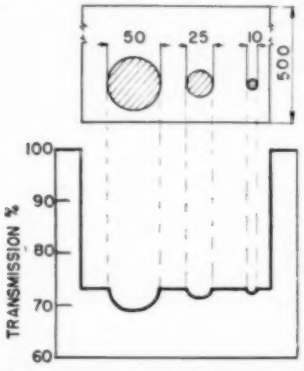

Figure 4. Transmission of 1.3 Å roentgen rays through a section 500 micron thick of soft tissue containing vessels 50, 25 and 10 micron wide filled with 50 % Neoprotosil.

Silver iodide has been used as a contrast, inter alia by BARCLAY, in micro-arteriography. Figure 4 shows schematically the transmission of a qualitatively heterogeneous roentgen beam having the effective wavelengths in the range 0.9 to 1.3 Å through a tissue where silver iodide is used as a contrast in the capillaries. Of course harder roentgen rays may be used to visualize the capillaries but the harder the roentgen rays the stronger the scattering and

other phenomena which may spoil the quality of the image.

The sharpness of the microradiographic image depends on several factors. The geometrical unsharpness, as illustrated in figure 5 a, depends on the following factors: the size of the focal spot and the distances between the focal spot, the sample and the photographic emulsion. The geometrical unsharpness can easily be reduced to 1 micron or less. Blurring of the image due to movements of the sample may become disturbing but may be eliminated by proper attention to this detail. The thickness and the granularity of the photographic emulsion are the ultimate limiting factors of the resolving power. The best emulsions, Lippmann-film (Gevaert, Antwerp), Eastman Kodak Spectroscopic plates 548 and 649 and Kodak Maximum Resolution plates have a resolving power of 500 to 1,000 lines per mm, which is sufficient for most microangiographic work. Other factors influencing the sharpness of the image of a capillary filled with roentgen contrast, are shown in figure 5 b. If the contrast filled vessels lie close to the photographic emulsion the secondary characteristic radiation from the contrast may obscure the image. This factor operates maximally at the edges of the contrast filled vessels. The internal unsharpness in the photographic emulsion depends partly on the range and azimutal distribution of the photoelectrons emitted on the passage of roentgen rays through the sample and emulsion. The scattered roentgen rays may also contribute to the unsharpness in the image. The range of the photoelectrons increases with their energy as shown in figure 6, which is plotted from the numerical values from LEA (1946). The highest energy of the electrons corresponds without refinements to the voltage for the short wavelength limit of the continuous roentgen spectrum. However, it is difficult to predict theoretically the quantitative influence of the secondary characteristic and scattered

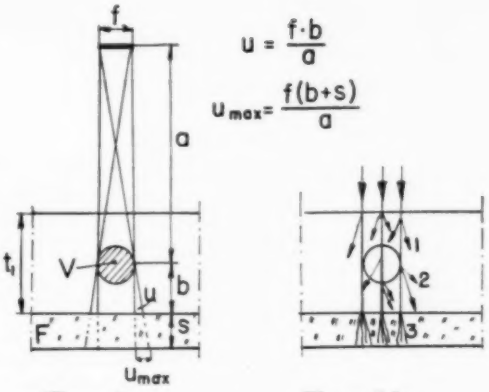

Figure 5 a. Figure 5 b.

a. The geometrical unsharpness, U, in the microradiographic image of a contrast filled vessel V. F is the film emulsion which has the thickness S.

b. Unsharpness due to: 1, roentgen scattering in the soft tissue: 2, characteristic secondary radiation from the contrast and radiation scattered in the contrast; 3, range and distribution of photoelectrons in the photographic emulsion.

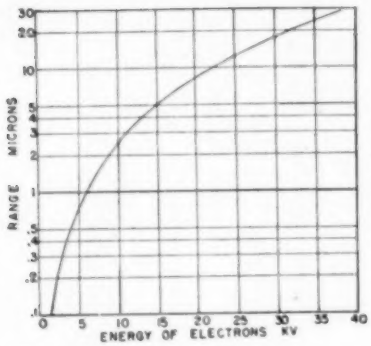

Figure 6. Range of photoelectrons in a medium with the specific gravity 1. (Plotted from LEA.)

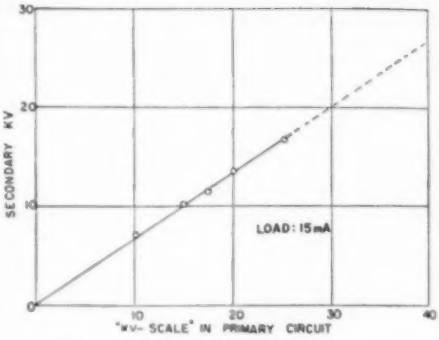

Figure 7. Effective secondary voltage as function of the 'kV-scale' in the primary circuit.

radiation, as well as of the photoelectrons, on the sharpness of the microradiographic images. In microradiography of thin tissue sections with 1—5 kV roentgen rays, these complicating factors are negligible but for higher voltages and thicker specimens they may become progressively disturbing. Test experiments on the quality of the microradiographic images have to be performed in each case, especially when high voltages are being used.

The theoretical aspects, briefly presented above are generally valid for vessels exerting a positive or negative contrast to the tissue. The vessels in hard tissue, such as bone, are better visualized with their negative contrast, *i. e.* by examining dried specimens.

Equipment and the Quality of the Radiation Used

A North American Philips roentgen diffraction unit, type no. 12031, was utilized as a source of radiation. Tubes with Lindemann-windows and molybdenum or copper targets were used. As the high voltage in this roentgen equipment is indicated by a scale on the variable transformer in the primary circuit of the high voltage transformer, it was necessary to calibrate the secondary voltage. Generally the experiments described later were performed with a tube current of 14—16 mA and therefore the calibration curve shown in figure 7 was registered with 15 mA through the roentgen tube. The current dependence of the high voltage is not very high in the region 14—16 mA. As the unit has no condensers the peak voltage is higher than that given in figure 7.

The effective wavelength was calculated by measuring the absorption of the heterogeneous roentgen beam in different materials.

The measurements were performed: 1, by using a fluorescent screen in connection with a photomultiplier tube (cf. figure 8) and 2, photographic-photometrically. Figure 9 shows the extinction of the roentgen beam in cellulose acetate and in aluminum as determined with the

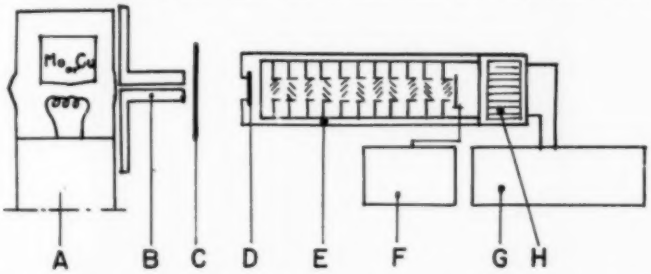

Figure 8. Equipment for measuring the intensity of roentgen rays. A roentgen tube; B pinhole; C sample; D silver activated Zn S fluorescent screen; E photomultiplier tube (E. M. I. Res. Lab., Hayes, England) Type 5060; F galvanometer; G high voltage for the photomultiplier tube; H voltage divider.

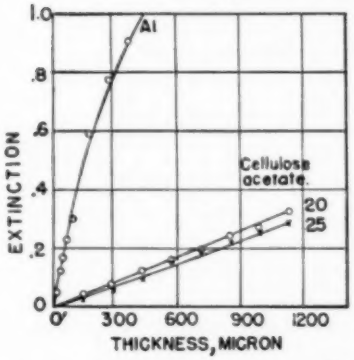

Figure 9. The extinction $\left(^{10}\log \frac{I_0}{I}\right)$ of 20 and '25 kV' (primary scale) roentgen rays in cellulose acetate and aluminum ('20 kV'). Cu-target.

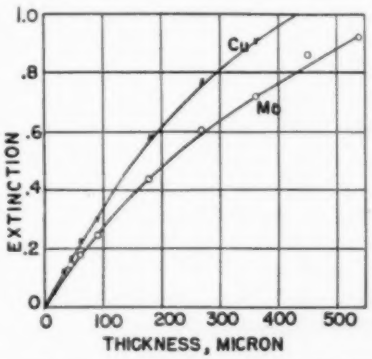

Figure 10. The extinction of '20 kV' primary scale roentgen rays in aluminum using two tubes with copper and molybdenum targets. The window of the latter tube is thicker.

fluorescent screen-photomultiplier. The effective wavelength fo extinctions up to about 0.4 and calculated from these curves is about 1.2 Å. The extinctions of the sample in a typical microangiographic experiment are expected to be about 0.1 to 0.3. Figure 10 shows the comparison between the absorption of the radiations from the tubes with copper and molybdenum targets, run with the same voltage. The higher trans-

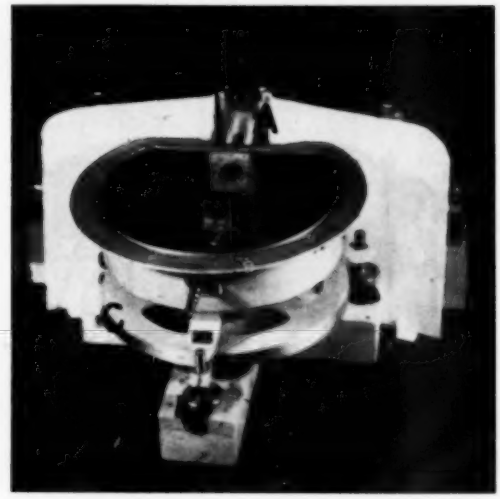

Figure 11. Device for microangiography. A roentgen tube; B sample-photographic plate. C scale to read the tilting angle when taking stereo-microradiographs.

mission of the radiation from the Mo tube is mainly due to the strong filtration in the thick window. At the wavelength used, '20 kV' on the primary scale which corresponds to about 13 kV effective secondary voltage (figure 7) Mo K radiation is not excited. In case of the Cu tube, however, the Cu K radiation is excited, thus softening the effective radiation.

The effective wavelength of the radiation was also measured photographic-photometrically in the straight portion of the density curves (cf. figure 12). Aluminum and silver were used as absorbers. From the measurements the effective wavelength was calculated to 1.3 Å for '25 kV' radiation from the copper tube (Mo-tube 1.2 Å). For higher voltages, 40 to 45 kV on the primary scale, only slightly different values were obtained. This fact may be due to the decrease in sensitivity of the photographic emulsion for decreasing wavelengths of the roentgen rays. The effective wavelength 1.3 Å gave experimentally the mass absorption coefficient 35—40 for Neoprotosil. The theoretically calculated mass absorption coefficient is about 37 for Neoprotosil at 1.3 Å, monochromatic radiation.

Summarizing the experiments it may be concluded that during the experimental conditions used the *effective wavelength* of the roentgen radiation is about 1.0—1.3 Å.

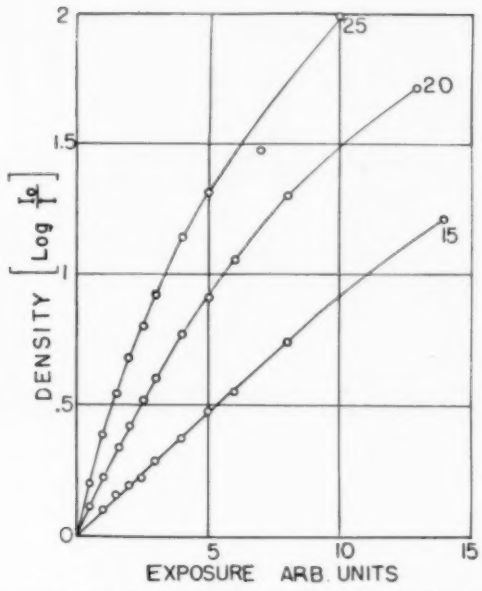

Figure 12. Density-exposure curves for Kodak Maximum Resolution plate. The figures on the curves indicate the voltages on the primary scale. Cu-target.

The device arrangement for microangiography is shown in figure 11 and includes a Siegbahn vacuum spectrograph. The focus to emulsion distance was 24 cm. The apparatus was not evacuated. The absorption of the radiation used for the experiments (25 kV on the primary scale) was measured to 10 % in 24 cm air (atmospheric pressure, room temperature) thus only slightly reducing the roentgen intensity. The scattering in the air did not seem to influence the sharpness of the microradiographic image. The samples were mounted on thin mica sheets (20 to 40 micron in thickness) which were pressed against the photographic emulsion. The sample-plate could be tilted and the vertical axis of rotation lay in the emulsion plane. Thus it was possible to register stereoscopic microradiograms.

Kodak Maximum Resolution plates or Eastman Kodak Spectroscopic plates 548 or 649 proved to be suitable materials for recording the microradiograms. Density curves for the Maximum Resolution plates are shown in figure 12. From this figure it can be seen that there is a linear relationship between density and exposure up to a density of about 0.5. In this region which is suitable for the subsequent photomicrography equation

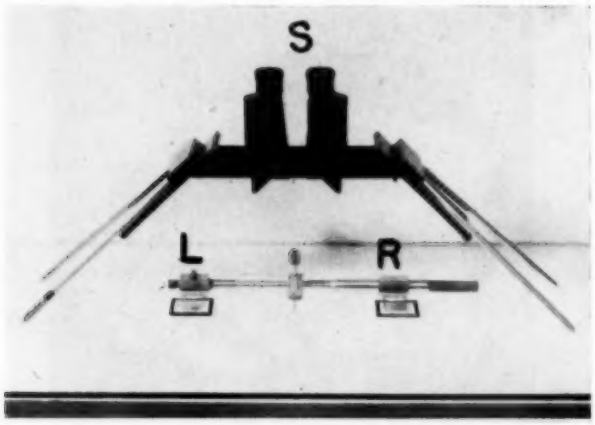

Figure 13. S stereolup (NIFE) used to observe the two enlarged microradiograms L and R when studying the three dimensional arrangement of the capillaries.

5 is valid. In the density region 1.0 to 1.5 a gamma value of about 1.5—2.5 is obtained. This region is suitable for microscopic inspection of the microradiographs. Naturally the values given are valid only under the developing conditions used in our experiments. The difference between two roentgen intensities is amplified by the gamma value of the photographic emulsion. If small differences in roentgen intensity (little differential absorption) are recorded it is preferable to work with a strongly exposed emulsion as the gamma value increases up to a certain density value.

According to NEEFF (1925) the smallest density difference that can be observed with the naked eye is 0.005 at a background density of 0.7—0.9.

For good stereoscopic vision of the enlarged microradiograms one must use the proper tilting angle of the sample-plate to suit the intended magnification. The tilting angle depends furthermore upon the distances between focus, sample and emulsion (cf. ENGSTRÖM 1951). With the equipment used and for a final magnification of $\times$ 50 to $\times$ 75, the tilting generally was about 7° to 9° in each direction from the normal incidence. For details see BERTHOLD (1941), ENGSTRÖM (1951), MÜLLER (1951).

The microradiograms were enlarged $\times$ 8 to $\times$ 20 by photomicrography and viewed in a stereolup with 4 times magnification. Figure 13 shows the arrangement for the stereoscopic examination of vessels visualized by microangiography.

Technique of Applying the Roentgen Contrast

In autopsy specimens relatively concentrated contrasts can be introduced into the capillaries. One of the factors limiting the concentration of injectable contrast is the viscosity of the solution. Induced osmotic changes in the vessels must also be taken into consideration. In the present work Neoprotosil (Parke, Davis & Co.) solutions were used as roentgen contrast according to BARCLAY's recommendation. The dried contrast contains 18—22 % silver iodide (Ag, $Z = 47$, J, $Z = 53$) and 80 % protein (H, $Z = 1$, C, $Z = 6$, N, $Z = 7$, O, $Z = 8$). Solutions containing 50 % contrast (weight/volume) can be injected into the capillaries. This contrast solution contains 10 % silver iodide.

A small percentage of an element with atomic number around 50 will give good contrast in the smallest capillary nets with the roentgen radiation used. Elements with higher atomic numbers may give a certain improvement in detailed structure of the capillary. The problem of the ideal contrast will be treated in a later communication.

The contrast was injected intra-arterially into surgical specimens and into heparinized and slain animals. The injection of contrast was continued until most of the blood was emptied through the opened veins. Concentrations of Neoprotosil ranging from 10 to 50 % were used.

In living animals the concentration of the contrast in the blood must be relatively low in order not to induce pathologic vessel and tissue reactions; elements with high atomic numbers must therefore be used in the contrast. Naturally it must not be poisonous. Thorotrast (Heyden) seems to be a suitable medium. The solution contains 25 % thorium oxide (thorium, $Z = 90$) and remains in the circulation for some time. This contrast was employed intravenously (intracardially in small animals).

Tissue samples were removed either in narcosis or after sacrifying the animal.

The tissues were microradiographed in the wet state or after routine histologic preparation. Sections 0.1 to 2 mm thick were cut. The sections of embedded tissues were not deparaffinized when examined. The examination of wet tissue slices has the obvious advantage of being rapid and simple; the more elaborate histologic preparation has other merits: the contrast remains in the opened vessels, shrinkage and movements of the sample are relatively small and several exposures with different qualities of radiation may be made on one and the same section. The sections may also be stored for other types of investigation.

Results and Discussion

In this communication only a few illustrations of the possibilities of the microangiographic technique will be given. The various medical problems which are being investigated with microangiography will be published elsewhere.

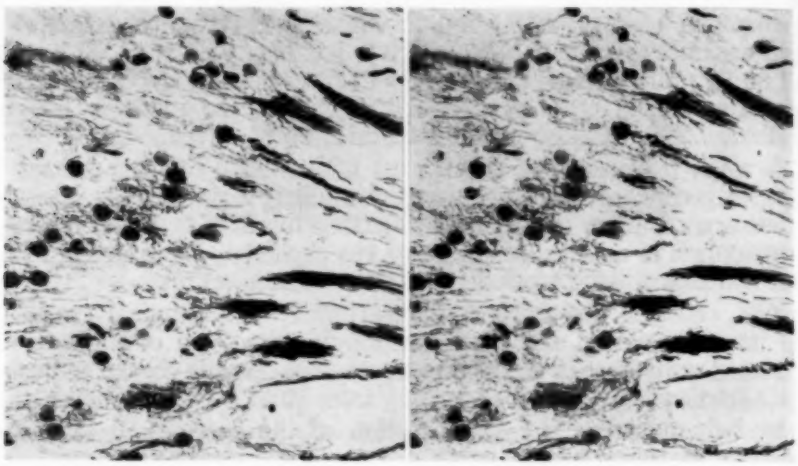

Fig. 14. A stereo-pair of enlarged microangiographs from a dog's kidney injected with 50 % Neoprotosil. Note the glomeruli and the capillaries. Enlargement × 17.

Figure 14 shows photomicrographs of stereo-microradiograms from a 0.5 mm thick section of a dog's kidney injected with 50 % Neoprotosil. The black areas indicate the roentgen opaque material (contrast). Viewed in the stereoscope the three dimensional arrangement of the minute blood vessels may be studied. The resolution in the photograph is about 2 microns (figure 15).

As mentioned earlier in this paper the blood vessels in bone tissue should be demonstrated by their 'negative' contrast. An enlargement of a microradiogram of a 0.3 mm thick, longitudinal section of a human femur in which the Haversian canals (white in the picture) are clearly visible, is shown in figure 16.

The advantage of microangiography, in comparison with optical 'clearing' methods, lies in the fact that thick specimens may be examined especially when stereoscopic registration is used. It also seems possible to obtain a 'physiologic' status of the capillary circulation by using con-

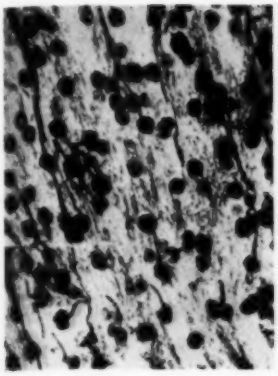

Figure 15 a.

Figure 15 b.

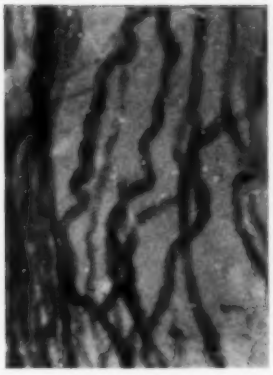

Figure 15 c.

a. Survey of a section 500 micron thick of a dog's kidney injected with Neoprotosil. Note the capillaries. × 17.
b. Two glomeruli — high magnification. × 122.
c. The vasa recta — high magnification. × 122.

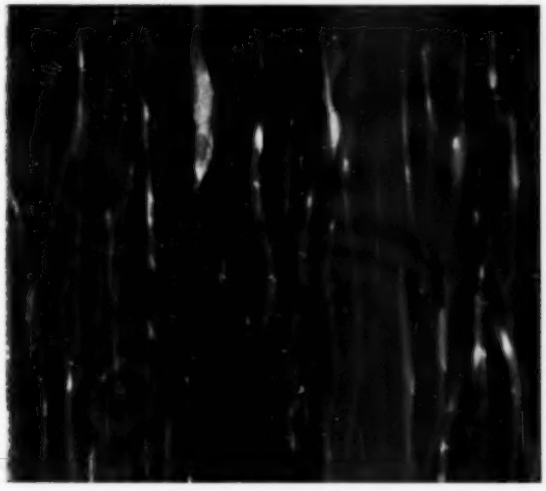

Figure 16. The distribution of Haversian canals (white) in bone tissue. The canals are visualized by their negative contrast. Enlargement × 17.

trasts such as Thorotrast and obtaining specimens from living animals by biopsy. Such experiments are in progress. In conclusion it may be said that microangiography appears to be a useful method for studying the capillary circulation in tissues under normal and pathologic conditions.

SUMMARY

The theoretical basis for stereoscopic microangiography and its practical applications are discussed.

ZUSAMMENFASSUNG

Die theoretischen Unterlagen der stereoskopischen Mikroangiographie und deren praktische Anwendbarkeit werden diskutiert.

RÉSUMÉ

Étude des bases théoriques et des applications pratiques de la microangiographie stéréoscopique.

REFERENCES

Barclay, A. E.: Micro-arteriography. Blackwell Scient. Publ., Oxford 1951.

Berthold, R.: Vergrösserte Röntgen-Raumbilder von Metalldünnschliffen. Metallwirtsch. 20 (1941), 694.

Bohatyrtschuk, F.: Über Ergebnisse der Mikroröntgenographie. Acta radiol. 25 (1944), 351.

Engström, A.: Quantitative micro- and histochemical elementary analysis. Acta radiol. Suppl. LXIII (1946).

— Microradiography. Acta radiol. 31 (1949), 503.

— Stereomicroradiography. Acta radiol. 36 (1951), 305.

Lea, D. E.: Actions of Radiations on living cells. Cambridge University Press 24 (1946).

Müller, E. A. W.: Röntgen-Mikrographie. Archiv. Techn. Messen. Lieferung 173 (1950).

Neeff, Th.: Metalluntersuchung mittels Röntgenstrahlen. Zsch. techn. Phys. 6 (1925), 208.

Tirman, W. S. and H. W. Banker: A Simple Method of Microradiography Using Ordinary Diagnostic X-ray Equipment. Science 113 (1951), 530.

—, Taylor, C. E., Banker, H. W. and Caylor, T. E.: Microradiography. Its Application to the Study of the Vascular Anatomy of Certain Organs of the Rabit. Radiology 57 (1951), 70.

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ABDOMINAL AORTOGRAPHY

with special reference to its complications

by

Harry Larsson and *Andreas Palmlöv*

REYNALDO DOS SANTOS and collaborators A. C. LAMAS and J. P. CALDAS presented their experiences in abdominal aortography (ao.), in 1929 (cited from R. DOS SANTOS 1933). In 1937 R. DOS SANTOS published a more detailed paper, in which he maintained the great advantages and harmlessness of the method. Although an occasional paper appeared, it seems that little attention was paid to this method elsewhere. During recent years a few authors have again adopted the method, and reported excellent results. (NELSON, WAGNER, KELLER-DOSS, WEYDE, LINDSTRÖM, CEDERMARK-HENSCHEN-LINDBLOM, OLSSON.)

During the early years R. DOS SANTOS reported instances of serious complications and even fatalities, owing to the contrast medium used or to hepatic and renal insufficiency.

A distinct warning against the method was issued by HENLINE and MOORE 1936 following an experimental study on 19 dogs in which the aorta was punctured from behind. Five died from traumatic haemorrhage shortly after the aortic injections, and three apparently from the toxicity of the drug. DOS SANTOS has pointed out, however, that the risk of haematoma formation following the puncture is greater in dogs than in human beings and that the former are more susceptible to iodine compounds. Conclusions from such animal experiments should therefore be drawn with reserve (DOS SANTOS 1947).

Among the later authors NELSON reported moderate degree of iodism in 4 cases in which sodium iodide was used.

ANTONI & LINDGREN described a case of paraplegia and paresis of the bladder and rectum, which was considered to be caused by com-

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pression of the aorta by a pillow placed under the abdomen. The contrast used in this case was 70 % diodrast.

Exact statements on the number of investigations and complications is not to be found in the literature. However, after an abstract from a paper by MELICK and WITT on abdominal aortography in the Year Book of Urology 1948, LOWSLEY makes the following comment: "Several human fatalities resulting from abdominal aortography have not reached the literature . . ."

Experimental Investigations

Most authors have used sodium iodide as a contrast medium and have thereby obtained extremely good shadows. Since, however, this substance is rather toxic and is known to exert a markedly irritating action on the vascular endothelium, we have absolutely refused to use it. In its place we have exclusively employed Umbradil (Astra) or Dijodon (Leo) henceforth referred to as c. m. = contrast medium, *i.e.* preparations corresponding to diodrast.

The possible dangers from a c. m. comprise allergic reactions due to the preparation — which in our cases we have regarded as excluded beforehand by intravenous urography or arteriography — and toxic actions upon the parenchymatous organs, particularly the kidneys and liver. As for the blood vessels, irritation of the intima as well as secondary thrombosis must be considered.

The very low toxicity of the c. m. in humans is clearly demonstrated by clinical experiences in cardioangiography (ROBB & STEINBERG, SALÉN & WIKLUND etc.) in which a 70 % solution is rapidly injected in still larger quantities than those we use in ao.

In order to obtain some facts regarding the safety margin by determining the lethal dose in animals, experiments were carried out by the authors on rabbits.

4—7 ml per kg body weight of a 60 % solution was injected intravenously into 5 animals. All of them survived. In another 5 cases a 70 % solution was injected. The 9 animals which received from 1 to 7 ml per kg body weight survived as did one animal in which 10 ml per kg was injected. Both animals injected with an amount equal to 8—9 ml/kg died, however.

The solutions were injected into a vein of an ear. The speed of injection was not very rapid — about $^1/_3$ ml per second — as these solutions are difficult to inject in this manner more quickly. When the quantities injected were so large as to cause the death of the animal, this was usually manifested by generalised spasm, opistothonus, expiratory dyspnoea and often oedema of the lungs. The same signs were re-

corded by LASCH & ROLLER after injections of highly concentrated solutions of various sodium or lithium salts; the effect need not therefore be regarded solely as a specific action of the umbradil molecule. We have in rabbits also observed death in convulsion after the injection of hypertonic glucose solutions, although in larger doses. LASCH and ROLLER regarded the signs to be caused by 'Verschiebung des Ionengleichgewichts im Blute'. In their experiments they were often able to prevent the spasms and death by the injection of calcium salts.

In our experiments the doses injected were very large. The lethal doses in the rabbits exceeded 7 ml/kilo. If conclusions are permissible from these experiments, they seem to imply that the margin of safety as regards general toxicity is fairly large.

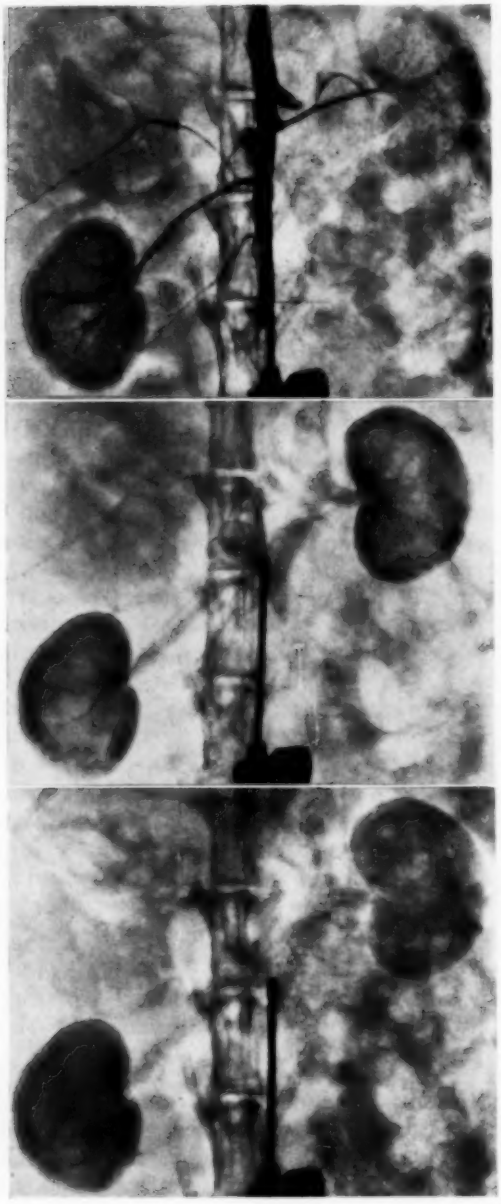
As for the action upon the arteries, highly concentrated solutions of c. m. are known to cause arterial constriction (HOLM among others, 1944) and a similar reaction is likely to arise within the kidney. In an experimental study of cerebral angiography, BROMAN & OLSSON (1948) have shown that strong solutions cause disturbances of the permeability of the vessels. Using 70 % of dijodon for mediastinal phlebography, we have sometimes observed thrombophlebitis, a complication also encountered by SALÉN & WIKLUND, 1948. When the solution is injected into a large vessel such as the aorta, the dilution, however, is very rapid.

Since the kidney is the excretory organ for a c. m. the temporary overload may put a strain on its function. If, by an unfortunate accident, all or most of the radiopaque solution should be injected into one renal artery, this might result in renal injury. Thus ao. should be considered as contraindicated in cases with poor renal function, and the same in all probability applies to cases with liver damage.

The arterial and venous phases of the circulation in the kidneys of experimental animals has been studied by TRUETA etc., using thorotrast. There have, however, been no investigations with a water-soluble contrast concerning:

1) the period of the arterial phase, when the vascular branches are most conspicuous
2) if with a dose approximately corresponding to that used in man, the vein tree could be observed and thus
3) whether properly timed exposures might give information regarding the circulation in the kidneys additional to that obtained by the roentgenologic representation of one phase only.

Under urethane or nembutal anaesthesia, with the occasional addition of ether, laparotomy was performed and a cannula inserted into the abdominal aorta from below with the tip close to the origin of the renal arteries; the superior mesenteric artery was ligatured. During the in-



a.

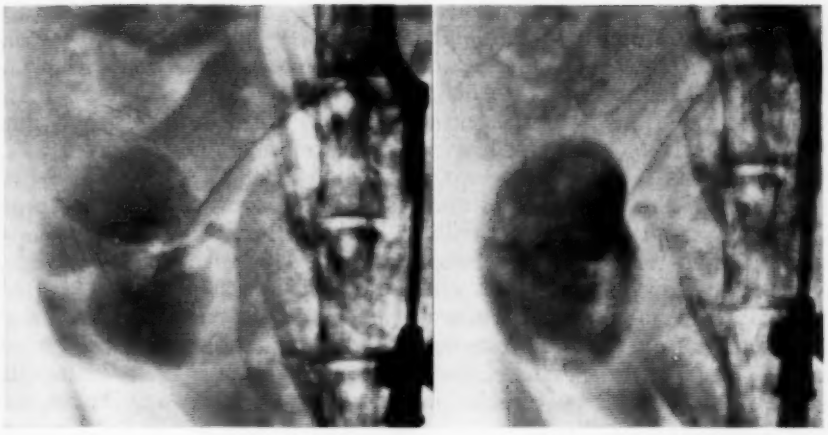
b.

c.

jection of the contrast solution roentgenograms were taken in series of 6, the time being registered by means of an electrocardiograph.

In 8 such experiments 5—7 ml of 70 % Umbradil were injected in 2—3 seconds. In normal animals the arteries appeared most clearly at an early stage of the arterial phase, before they were partly obscured by the rapidly occurring accumulation of contrast in the finer vessels of the cortex. The latter caused a very heavy and homogeneous opacity of the cortical layer, sharply defined against the medulla, which showed a fainter contrast. This sharp difference between the cortex and medulla seen early in this primary opacity of the cortex, was reduced as the c. m. commenced to be transferred to the veins (Fig. 1 a—c). The contrast began to be visible in the kidney vein 2—4 seconds later than in the arteries and in some cases but by no means constantly, distinct intrarenal vein trunks could be observed.

Fig. 1. Normal aortogram of a rabbit. (a) Arterial stage, (b) venous stage and (c) late venous stage. Interval of 3.1 sec. between (a) and (b) and 18 sec. between (a) and (c).



a. b.

Fig. 2. Aortogram of the same rabbit as in Fig. 1, in a state of shock. (a) Arterial stage, (b) 3.2 sec. later.

After the contrast had disappeared from the arteries the veins were distinctly visible for remarkably long times, *viz.* in three cases for 6 seconds and in one case for 15 seconds. This strikingly protracted venous outflow may be due to temporary stagnation of the blood within the kidney.

The foregoing remarks refer to the intensification of the renal shadow due to the filling of the vessels with contrast medium. The increasing contrast load of the excretory cells and channels will in time also cause a density of the renal shadow (nephrographic effect HELLMER).

In order to outline the kidney vein regularly in the film it was necessary to use the large contrast quantities mentioned above. In any case 2—2.5 ml were found to be insufficient with the technique employed.

In one of the experiments a great deal of the animal's blood was lost accidentally through the aorta. Forty minutes earlier an examination employing 6 ml of 50 % solution of Umbradil had been made and normal films obtained. Soon after the loss of blood, when the animal was in a state of shock, 6 ml of the same contrast were again injected. The films now obtained were entirely different from the normal (Fig. 2 a & b) in so far as the contrast never reached the cortex in the usual way but on the other hand the vessels in the medulla showed a comparatively increased contrast. It is true that part of the shadow in the last series was caused by the excretion proceeding continuously after the first dose of Umbradil. That the main part of the shadow was caused by filling up

of the vessels is proved by control films taken immediately before the last series. The appearances directed our thoughts to the shunting mechanism of the circulation in the kidneys, such as was shown by TRUETA and his collaborators in their monograph of 1947. We were inclined to interpret the films as representing a state of shock through bleeding associated with lowering of the blood pressure, chilling and operative trauma.

This experimental method unfortunately causes considerable operative trauma and a concurrent chilling of the abdominal viscera is almost unavoidable. We have, therefore, not proceeded with these studies as a means of investigating such circulatory problems further.

From the above experiments we may conclude that the margin of safety of the c. m. in the concentration and quantities we use for ao. in man is large; and further, that the possibility of demonstrating the venous stage of the renal circulation is favoured by increasing the amount of contrast and by frequent serial exposures over a rather long period, since the venous phase seems to be of varying length.

Complications and Possible Dangers from ao. in Man

A detailed description of the puncture with the errors which may occur and the dangers is found in R. DOS SANTOS' paper of 1937.

We use a straight needle, 12—14 cm in length and with an outer diameter of 1.2—1.5 mm.

We always use some form of anaesthesia: spinal in a few cases but intravenous evipal in the majority. After completion of the roentgen procedure most patients are given an infusion of about 500—800 ml of 5 % glucose or Dextran (Pharmacia, Sweden).

In all cases we employ 30 ml of a 70 % solution of Umbradil (Astra) or Dijodon (Leo).

The film series are made during the injection and usually consist of three films at intervals of two—three seconds, the first being made after the injection of about 10 ml of contrast. In some cases elastic tourniquets were applied very tightly around the patient's thighs in order to obtain more concentration of the contrast solution in the abdominal branches of the aorta. Since we have not been able to demonstrate any benefit from the use of tourniquets we have lately abstained from using them.

The injection of the contrast solution was in certain cases made with a pressure apparatus of similar design to the one described by R. DOS SANTOS and in others with a hand syringe. The injection of 30 ml of the contrast solution was performed in 6 to 9 seconds.

The following discussion on complications and failures is based on our experiences of 62 adult patients (16—74 years) in which ao. was

attempted. Some of these cases were preliminarily reported by PALMLÖV in 1947 and RUNSTRÖM in 1948. In three of the cases in which the aorta was difficult to locate, we abandoned the attempt after a short trial; surgical operations had been planned in any event beforehand, so the failures were of no clinical consequence.

We wish to stress that of the remaining 59 attempts, the contrast medium was, in 7, injected outside the wall of the aorta. With increasing experience and improvement of technique we consider that this can be avoided in most instances.

One of these cases had very severe pain in the region of the diaphragm for two or three hours and a slight stitch for two days. There was no fever but two days afterwards, roentgen examination of the lungs revealed a small pleural exudate in the costo-phrenic sulcus; recovery was uneventful. All the remaining 6 patients had remarkably mild symptoms, only a few complaining of slight aching pain in the back or epigastrium for a day or two; none was confined to bed on account of the mishap. Thus the injection of the c. m. outside the aorta does not in itself appear to cause serious consequences. A further attempt at the time is not advisable, but should be deferred for several days.

Besides the above-mentioned complications the contrast solution was on one occasion injected (with a hand syringe) near the origin of the *right* renal artery, which apparently received the entire amount (30 ml 70 % Dijodon Leo). (Fig. 3.) The patient was a woman of 39 years, under treatment for a small movable *left* kidney with pain, attacks of fever, increased sedimentation rate and urinary infection. On the following day, the temperature rose to 38 deg. C. but then returned to normal; the urinary output was 1,200 ml and remained normal; concentration test unchanged at 1.020; no albuminuria and no microscopical changes in the urine; no increase in NPN; blood pressure unchanged: 135; the urea clearance test before the examination was 127 and 114 on two occasions but was lowered to 61 the day after ao., no surgical intervention being carried out in the meantime. The figure was 72 about one month later. During this month a *left* nephropexy was performed and later on a *left* nephrectomy, since the kidney function was abolished after the nephropexy. After the last operation the patient made an uneventful recovery. On follow-up examination — 13 months after the injection — the patient felt well and had no urinary symptoms. Blood count, urine examinations (macroscopical and microscopical) and NPN entirely normal; sedimentation rate 4 mm; blood pressure 125—80; urea clearance test 91. Concentration test of the urine was not performed but the dilution was normal; 1.002. Urography: quite normal findings in the remaining right kidney. Thus apart from a temporary lowering of the urea clearance test, we had not been able to prove any untoward

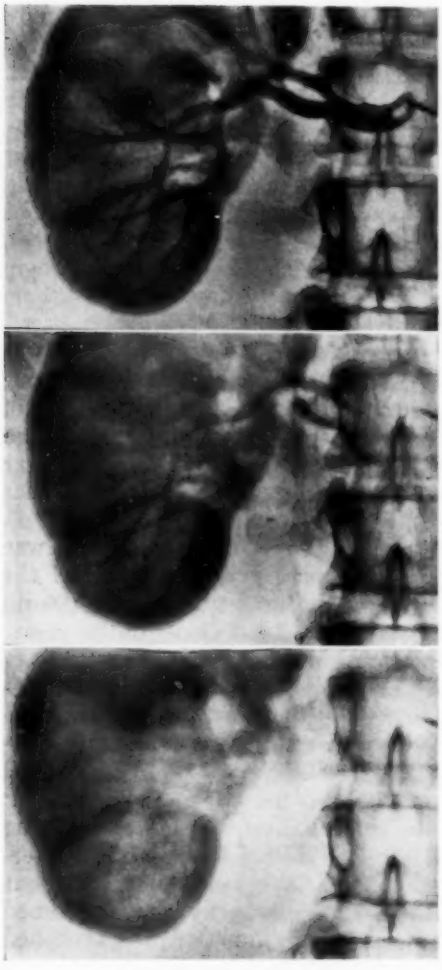


Fig. 3.

a. 30 ml of 70 % Umbradil unintentionally injected into the right renal artery. Arterial phase, but contrast already visible in the vein.

b. The arteries less contrast-filled. The kidney and the vein are more dense.

c. The opacity of the vein and the parenchyma more pronounced but the difference in density between the cortex and medulla less marked.

effect from the injection. Nevertheless this case is a warning. It is not unique as proved by MELICK and VITT's paper (1948) in which a solution of 80 % sodium iodide was reported as having been injected into one renal artery. They saw no serious sequelae in their case.

In one of our cases the needle, directed correctly towards the twelfth thoracic vertebra was bent and penetrated the aorta at the level of the renal arteries in the 'zone dangereuse' of DOS SANTOS. There was good contrast filling of the renal vessels and no untoward effect. The clinical result was excellent but the control of the puncture cannot be considered as satisfactory.

FARIÑAS (1946) obviously is not contented with the blind puncture of the aorta, for he advocates the retrograde route with a cannula inserted through the femoral artery. For renal diagnosis we regard this procedure as too complicated and involving certain risks of post-operative thrombosis.

The patients' reactions during and immediately following the injection have been very mild — in some instances a slight fit of coughing — with the exception of one case. A 42-year-old man, suffering from intermittent claudication, showed slight generalised spasm when recovering from the anaesthesia. He had showed these signs to a lesser degree during the induction of the anaesthesia and it is difficult to judge therefore,

whether the anaesthesia or the contrast injection should be held responsible. As this occurred in a patient with severe arterial disease, it is possible that the contrast injection may have contributed to the condition. The examination was performed with very tightly fitting tourniquets on the thighs and these perhaps should not be used in cases where the circulation in the lower extremities is defective (DOS SANTOS). The spasm disappeared within a few minutes after the administration of one ml ephedrine, and the patient had no untoward symptoms.

Immediately after the injection of the c. m. there is often, though not always, a temporary marked fall in the blood pressure, sometimes down to 70 mm Hg systolic. In all cases it has been restored within a few minutes. A similar reaction is sometimes found after large doses administered intravenously (ROBB & STEINBERG, where a discussion of the pharmacology of diodrast and a bibliography is found).

A slight aching pain in the back for one or two days after ao. was noted in one patient, whose temperature rose to 38 deg. C on the day following the examination and then gradually fell to normal in three days, when all her symptoms subsided. Temperatures up to 38 deg. C. were observed in three patients, but these returned to normal the day following the injection. One patient on roentgen examination on the third day showed a small atelectatic area in the lower field of one lung. He underwent nephrectomy for a hypernephroma on the sixth day and made an uneventful recovery; there was no fever and no subjective symptoms. Naturally the complications in the last-mentioned cases might be attributed to the anaesthesia. No patient has been confined to bed from aortographic sequelae.

Along with the aortographies we have performed certain laboratory tests in order to evaluate possible toxic actions upon the kidneys and the liver.

The daily output of urine (38 cases) showed no decrease. Since most patients were given an infusion of glucose or dextran and since the c. m. exerts a diuretic action, the quantity on the day following ao. has often been a little higher than before.

The concentration test of the urine (25 cases) as a rule performed two to three days after ao., showed no change.

During the period of excretion of the c. m., the specific gravity of the urine is increased, owing to the weight of the contrast substance. In some instances the excretion of sodium chloride was determined and found to be markedly increased.

Traces of albumin were observed in one instance for three days after ao., but the patient had previously suffered from macroscopical haematuria, and therefore no positive conclusion could be drawn. In 24 cases examined for albuminuria none was found.

Microscopical urine examination (35 cases) showed no difference before and after ao. Casts have never been observed. NPN was tested in 37 cases before and generally two to four days after ao. and no difference was found.

The urea-clearance test was performed after ao. in 12 instances. Since the figures normally vary within wide limits we give the results in the following table. The test was usually performed within 3 to 5 days. Where more than one figure is given, these refer to determinations on separate occasions.

Table 1

Before	After	Before	After
127, 114	61, 72, 91	86	92
83	79, 74	65	102
62	42, 143	creat. 96	creat. 162
72	95	38, 61	74
		59	76
73	50, 68	101	122
52	44		

The first case in the Table was the woman in whom the contrast was injected into the right renal artery. As regards the remaining cases we consider that no kidney injury was demonstrable.

Concerning the kidneys it should also be mentioned that intravenous urography — not as a function test per se but for clinical purposes — was performed after a lapse of from one to thirteen months after ao. in 10 cases. No difference in the excretory power of the kidneys was demonstrated.

We attempted to estimate a possible toxic action upon the liver by the determination of urobilin in the urine (SCHLESINGER) in 8 cases. In none was the test positive, unless so immediately beforehand. Jaundice was never observed nor the icterus index increased, nor was any other clinically demonstrable toxic action upon the liver found. Ao. was never performed in jaundiced patients.

In cases of progressive renal disease the possible danger is difficult to evaluate. We had one case in which ao. was performed to exclude the possibility of a renal tumour. A man, 37 years old, had suffered repeated attacks of severe macroscopic haematuria during the preceding seven months. He had been under observation for a long period in both the medical and surgical departments. Repeated descending and ascending pyelographic examinations were indefinite and repeated cystoscopy failed to reveal the source of the bleeding. The blood pressure was 160. Aortography satisfactorily excluded the possibility of a renal tumour in as

much as it showed regular distribution of even the smaller arterial branches in the kidneys and a uniform opaque rendering throughout the parenchyma. There was no untoward reaction to the examination and the immediate subsequent course was uneventful. However, the disease was progressive, and three months later the patient still continued to bleed periodically. His condition was about the same as before ao., although the NPN had risen to 50. The blood pressure remained unchanged (165/100). Nineteen months later the patient still suffered from haematuria and was uraemic with a NPN at times as high as 150. However, there was no further rise in the blood pressure. This was certainly a serious case from the beginning and we consider our examination to have been justified. We have no reason to suppose that the disease was unfavourably influenced by ao., although this possibility cannot be entirely excluded.

Post-mortem examinations have been performed in four cases. One was a patient with a hypernephroma with metastases in the brain and who died 5 months after ao. and nephrectomy. Another was a patient who died 17 months after ao. and resection of the bladder for carcinoma. No trace of the aortic puncture could be found in these cases and no macroscopic signs of thrombosis or vascular irritation.

The third case, a patient with hypernephroma and metastases, died 3 days after nephrectomy and 7 days after ao. We were not able to locate the site of the aortic puncture but after careful search, a small blood-stained area, measuring about 3 × 4 cm was found in the connective tissue behind the aorta. There were large tumour masses invading the vena cava, and further small metastases were found in both lungs. The aorta with its abdominal branches and the iliac arteries presented smooth intimal surfaces without any macroscopic signs of thrombosis or irritation.

The fourth case was a man of 54 years, suffering from severe heart failure with an embolus at the aortic bifurcation; any attempt at embolectomy was out of the question owing to his poor condition. This case is mentioned here merely for the evaluation of the possible dangers of the puncture. It is the only attempt we have made at a therapeutic aortic injection. A solution of 1 % novocain was injected in order to try and relax the arterial spasm. One hour prior to the injection, the patient had received 100 mg heparin intravenously; following it, the administration of the drug was continued. Death occurred about 18 hours later from cardiac failure. In spite of the heparinisation, a small extravasation of blood measuring about 5 × 4 cm × a few mm was found in the connective tissue behind the aorta on post-mortem examination. Much larger haematomas often occur after the puncture of a cubital vein. In these 4 cases the puncture was made with a 1.2 mm needle.

We had clinical evidence of haematoma formation on one occasion. This occurred in one of the three cases in which, owing to difficulty with the puncture, no contrast was injected. Whilst recovering from the anaesthesia, the patient complained of pain in the back. On roentgen examination a few hours after the puncture a small exudate was found in the left costophrenic sulcus. As it was not reasonable to assume that a pleural effusion could have formed within this short interval, the shadow was interpreted as being caused by haemorrhage. Because of the pain, the patient was given morphia but no other treatment was necessary and the symptoms vanished within a day; recovery was uneventful. In this case the puncture was made with a needle of 1.4 mm outer diameter and must have reached the aorta above the diaphragm.

Conclusions

The radio-opacity of the c. m. employed by us is much less than that of sodium iodide in the concentrations used in most of the earlier investigations. However, there have been but few cases in which the films have been useless by reason of poor visualization of all the vessels. The result has more often been spoiled through an unsuitable distribution of the medium; above all, this applies to the mesenteric vessels, which are sometimes the only ones to be clearly visualized even after a puncture at the correct level of the aorta.

A difficulty which we often encounter in ao. is the superimposition of vascular shadows which confuse the interpretation of the radiographs. For major pathological conditions such as large tumours, the phenomenon may be of no importance, but it can be of considerable inconvenience in the scrutiny of minor details within the renal parenchyma. This disadvantage is not avoided by increasing the density of the contrast solution.

In some cases the renal arteries were very poorly filled, in spite of a markedly opaque rendering of the aorta. The distribution of the contrast solution may to some extent be determined by the site of the needle within the aorta — whether it lies in the central or peripheral parts of the vessel, or near the exit of a large arterial branch. Furthermore, vascular reflexes may influence the distribution. DA COSTA & FAGUNDES (1947) have shown experimentally in dogs, that repeated ao. performed in exactly the same manner under standardized experimental conditions, may result in great variations in the distribution of the contrast between different vessels. Obviously it would be desirable to be able to direct the contrast mainly to that vascular area which we especially desire to examine. As for the renal arteries these can be better visualized by a

puncture near their origin, which, however, involves the risk of all the contrast solution being injected into one renal artery only.

Ao. with c. m. is followed by an opacity of the renal parenchyma which, as a rule, is more dense than in intravenous urography. This nephrographic effect affords valuable information about pathologic processes within the kidney; *i.e.* tumours, cysts, circulatory changes and the like and in this respect c. m. has great advantage over NaI. The ensuing contrast filling of the renal calyces and pelvis is also more pronounced.

DOS SANTOS emphasizes that the dangers of the method are connected with the contrast solution he uses (NaI) and not with the puncture. In our series the complications have not been due to the contrast medium but have resulted from the puncture and injection and have been of little clinical importance.

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SUMMARY

Experiments with rabbits show that the general toxicity of 70 % Umbradil is rather low and that the lethal dose far exceeds the quantity used in man.

A review is given of 59 cases of abdominal aortography (70 % Umbradil Astra or Dijodon Leo) with special regard to failures and dangers. The complications have not been due to the contrast medium but from the puncture; they had but little clinical importance.

ZUSAMMENFASSUNG

Versuche an Kaninchen zeigten, dass die allgemeine Giftigkeit des 70 % Umbradils ziemlich gering ist und dass die tödliche Dosis die bei Menschen angewendete Dosis weit übersteigt.

Es wird eine Übersicht über 59 Fälle von abdominaler Aortographie (70 % Umbradil Astra oder Dijodon Leo) gegeben, mit besonderer Rücksichtnahme auf die Misserfolge und die Gefahren. Die Komplikationen waren nicht durch das Kontrastmittel sondern durch die Punktion bedingt; sie hatten nur geringe klinische Bedeutung.

RÉSUMÉ

Des expériences sur des lapins montrent que la toxicité générale de l'Umbradil à 70 % est assez basse et que la dose léthale dépasse de beaucoup la quantité employée chez l'homme.

Les auteurs étudient spécialement, sur 59 cas d'aortographie abdominale (Umbradil à 70 % ou Dijodon Léo), les insuccès et les dangers. Les complications étaient dues à la fonction et non au produit de contraste; elles étaient cliniquement peu importantes.

BIBLIOGRAPHY

ANTONI, N. & LINDGREN, E.: Steno's experiment in man as complication in lumbar aortography. Acta chir. Scandinav. 98 (1949), 230.

BROMAN, T. & OLSSON, O.: The tolerance of cerebral blood vessels to a contrast medium of the diodrast group. Acta radiol. 30 (1948), 326.

CEDERMARK, J., LINDBLOM, K. & HENSCHEN, F.: Om diagnosen av njurinfarkt, särskilt med hjälp av aortografi. (Swedish.) Nord. Med. 10 (1941), 1793.

DA COSTA, C. & FAGUNDES, M.: Artériographie expérimentale (chien). XII:e Congrès Internat. de Chir. Londres 1947, p. 289. Imprimerie Médicale et Scientifique, Bruxelles 1948.

DOSS, A. K.: Translumbar aortography, its diagnostic value in urology. J. Urol. 55 (1946), 594.

FARIÑAS, P. L.: Retrograde abdominal aortography. Am. J. Roentgenol. 55 (1946), 448.

HELLMER, H.: Nephrography. Acta radiol. 23 (1942), 233.

HENLINE, R. B. & MOORE, S. W.: Renal arteriography, preliminary report of experimental study. Am. J. Surg., New series. 32 (1936), 222.

HINMAN, F.: Hydronephrosis in Dean Lewis, Practice of Surgery, Vol. 8, chapter 8. W. F. Prior Company, Inc. Hagerstown, Maryland, 1938.

HOLM, O.: Cinematography in cerebral angiography. Acta radiol. 25 (1944), 163.

LASCH, F. & ROLLER, D.: Über die Giftwirkung konzentrierter Salzlösungen. Arch. f. exper. Path. u. Pharmakol. 179 (1935), 459.

LINDSTRÖM, B.: Abdominal aortografi. (Swedish.) Finska läk.sällsk. handl. 92 (1949), 123.

MELLICK, W. F. & VITT, A. E.: The present status of aortography. J. Urol. 60 (1948), 321.

NELSON, O. A.: Arteriography in renal and abdominal conditions. J. Urol. 53 (1945), 521.

OLSSON, O.: Indikationerna för renal angiografi. (Swedish.) Svenska Läkartidningen 45: *1* (1948), 349.

PALMLÖV, A.: Abdominal aortography, especially with reference to renal diagnosis. Tr. Twenty-third meeting Northern Surg. Ass., p. 413, Ejnar Munksgaard, Copenhagen 1948.

— Abdominal Aortography, with Special Reference to Renal Diagnosis. Acta chir. Scandinav. 103 (1952), 165.

ROBB, G. P. & STEINBERG, I.: Visualization of chambers of heart, pulmonary circulation, and great blood vessels in man; practical method. Am. J. Roentgenol. 41 (1939), 1.

RUNSTRÖM, G.: Aortografi. (Swedish.) Nord. Med. 38 (1948), 934.

SALÉN, E. F. & WIKLUND, TH.: Angiocardiography in coarctation of the aorta. Acta radiol. 30 (1948), 299.

DOS SANTOS, R.: L'artériographie en série. Bull. et mém. Soc. nat. de chir. 59 (1933), 1.

— Technique de l'aortographie. J. internat. chir. 2: 6 (1937), 1.

— Artériographie et phlébographie. XII:e Congrès internat. de chir. Londres 1947, p. 263. Imprimerie Médicale et Scientifique, Bruxelles 1948.

FROM THE ROENTGEN DEPARTMENT (DIRECTOR: BENGT HOLMGREN), SABBATSBERG HOSPITAL, STOCKHOLM, SWEDEN

SOME OBSERVATIONS ON THE SHAPE AND COURSE OF THE FEMALE URETHRA DURING MICTION

by

Björn E. W. Nordenström

Many extensive histologic investigations of the female urethra have been published. Careful dissections and physiologic studies have clarified many of the anatomic and functional problems of importance to the understanding of normal miction in women. Serial sections of the urethra have also been made (15).

Comparably few studies of the shape and topography of the urethra during miction, have, however, been carried out. Roentgenologic technique is well suited for this purpose. In combination with comparative studies of casts of the urethrae in cadavera, it seems for the present to be the best way of obtaining information on these matters.

The Anatomy of the Female Urethra

Most textbooks of anatomy describe the female urethra as a truly distensible canal 2.5—4 cm in length. This is measured in gross sections in cadavera; the urethra of the living subject is said to be shorter (24).

The urethra arises as a small funnel-shaped opening in the lower anterior part of the bladder; it pursues a somewhat curved course with the concavity directed antero-superiorly and ends in the upper part of the vestibulum vaginae.

From the external to the internal meatus the urethra lies at an angle of 16 degrees to the anterior vaginal wall (15).

A small transversal fold of the mucosa of the anterior wall of the internal meatus is called the uvula vesicae. In addition the walls are lined by mucosa forming numerous longitudinal folds, one of which, situ-

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ated on the posterior wall, is prominent; it is termed the crista urethralis. The external orifice often possesses irregular lips forming a stellate, crescentic or cleftlike opening to the vestibule.

There are numerous small glands in the mucosa, some of which correspond to the prostata (12, 9). A sheet of smooth musculature arranged in an outer circular and an inner longitudinal layer is found external to the loose sub-mucosa. A well-developed plexus of veins lies between the two layers. Near the bladder neck the circular layer is more developed. The trigonum muscle of KALISCHER (14, 29) is of great importance and consists of smooth transversally arranged muscle fibres situated beyond the vesical mucosa and behind the meatus internus urethrae. From the outer muscular layer of the bladder smooth fibres pass down longitudinally to the posterior urethra, and are known as the muscle of Heiss. Together with the trigonum muscle it is said to form a loop which surrounds the anterior part of the bladder neck.

The middle part of the urethra is surrounded by the striated muscle of the urogenital diaphragm (triangular ligament) (6, 7). Its importance as a voluntary sphincter is emphasized (7, 8, 20); it partially covers the internal urethral sphincter and is called the sphincter urethrae membranaceae (11). It is also said to correspond to the external urethral sphincter in the male (5). The distal part of the urethra is surrounded by striated muscle fibres derived from the bulbocavernosus.

According to WALDEYER the posterior urethra is connected more loosely to the symphysis than the anterior urethra.

Intimate contact between the dorsal urethral wall and the vagina is established by the fibromuscular tissue of the fascia urethro-vesico-vaginalis of HALBAN. This contact is particularly firm in the lower part of the urethra (15).

The fibromuscular fascia pubocervicalis of BONNEY (2) or 'the pubocervical muscle sheet' is also of certain interest. This tissue runs from the postero-inferior part of the symphysis in the space of Retzius around the bladder neck to the cervix uteri. It is sometimes called 'the pubourethral', 'the urethropubic' or 'the puboprostatic' ligament. Contractions of muscle fibres within this fascial structure (pubovesical muscle 12) is said to cause an angulation of the urethra on the base of the bladder (27, 28). The existence of a puboprostatic ligament has recently been denied (10).

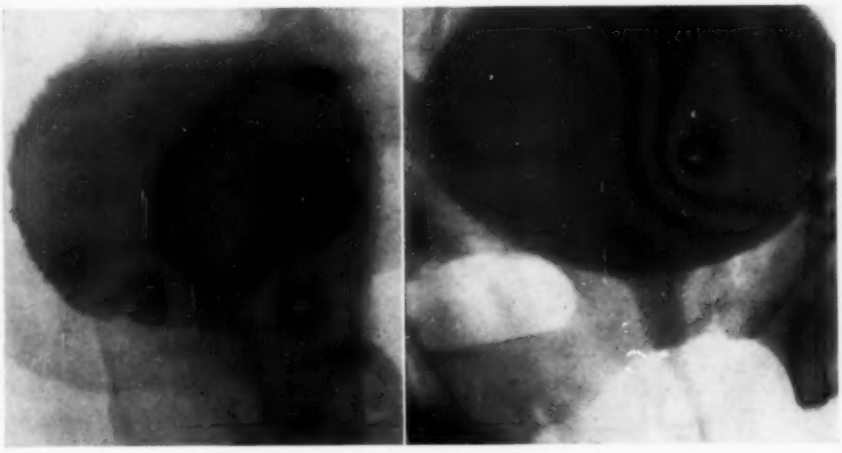
Previous Roentgenologic Investigations

An attempt to study the macroscopic anatomy of the female urethra by roentgenologic technique was made by TOMSEN (28).

He injected lipiodol through the external meatus, obtained films

in the oblique positions and demonstrated an antero-superior angulation of the posterior urethra in normal living subjects. The angulation was considered to be a function of the trigonum muscle and the muscle of Heiss. The middle and anterior parts of the urethra could not be examined by this method.

For examination of the course of the female urethra, a small light metal chain has also been used (28); lateral urethrograms were obtained and showed a slight posterior curvature or a straight course of the urethra.



a. b.

Fig. 1. Lateral (a) and oblique (b) views in urethrography in the same patient. The details of the urethra are more easily recognized in the lateral view.

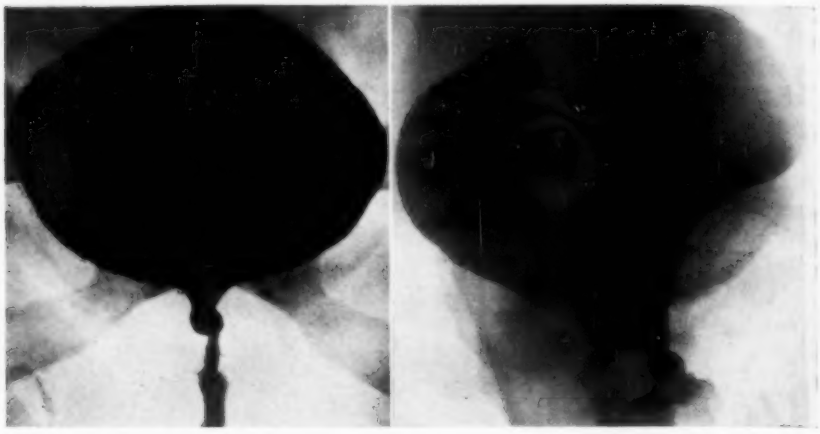
Own Investigations

By a technique previously introduced by the author (21) it is possible to examine the whole female urethra during micturition with the patient in the antero-posterior and lateral positions.

Although the lateral position is of more importance it is always necessary to obtain antero-posterior films.

In Fig. 1, a comparison is made between films obtained in the oblique and lateral positions of the same patient during micturition. Many details of the urethra are partly superimposed in the oblique position and the topography is difficult to analyse.

It soon became apparent that the shape and course of the normal female urethra did not quite correspond in certain details to the descrip-



a. b.

c.

Fig. 2. a) Normal urethrocystography. Anterior and b) lateral projection. c) Schematic drawings from Fig. 2. A tangential and funnel shaped posterior urethra is seen. The middle part of the urethra is considerably distended during miction; distally, a large navicular fossa. Posterior and anterior angulation of the urethra. m. e. = meatus externus.

tions in the textbooks of anatomy. It was also possible to confirm recent observations.

The shape and course of the female urethra during miction seems to be highly variable. It would therefore be necessary to examine a comparatively great number of healthy women of various ages as well as terminal pregnancies, in order to obtain a more definite opinion on these matters. Such a material is not the basis for this paper. The conclusions are drawn from findings in ten continent cases and are compared with the findings in 50 incontinent cases. Certain findings seem

to be common in healthy as well as in a great number of incontinent women and may be summarized as follows:

I. Observations also previously described by other investigators

1. The posterior urethra has a tangential course in relation to the bladder base in adults; it usually has the shape of a small oblique funnel.

2. The lumen is generally narrowed corresponding to the tip of the funnel of the posterior urethra.

3. The wedges of the external orifice often constitute a narrowing of the urethra.

4. An angulation or slight bending of the posterior urethra as previously described (30) was found; the concavity was directed ventrocranially.

II. Further observations

1. A middle part of the urethra is distinguishable. It appears as a spool-shaped dilatation during miction. In most cases it forms the widest part of the urethra.

2. Distally to the dilatation the urethra becomes considerably constricted over a length of up to one cm; this appears to be the narrowest part of the urethra during miction.

3. Distally to the constriction the lumen of the urethra rapidly widens just before the external orifice to become roughly circular in shape with somewhat flattened lateral walls; it appears rather similar to the navicular fossa in the male.

4. In the region of the narrowing (2) the urethra in most cases changes its course. This change may often be abrupt so that a dorso-inferior open angulation of the anterior urethra is formed.

Controls on Autopsy Material

In order to control the roentgenologic observations injections of rapid hardening materials were made into urethrae in autopsy material.

An agar preparation (Dentocoll — De Trey Frères, S. A., Zürich) used in dental surgery as a material for impressions was found suitable. This is a hydrocolloid of rubberlike consistency at room temperature; on immersion in boiling water it becomes soft and plastic.

The bladder of the cadaver was opened in situ. The urethra was then filled through the internal meatus by rapid injection of the impression material. After some minutes it was possible to remove a cast without destroying the urethral tissue.

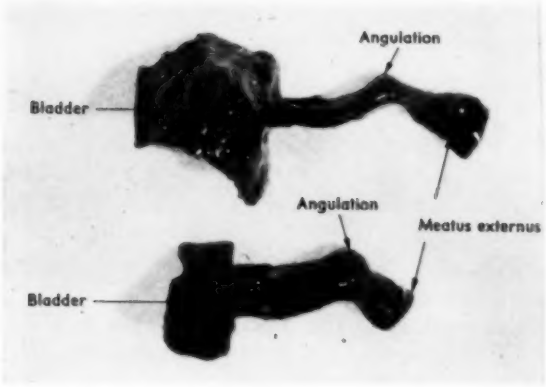


Fig. 3. Casts of female urethrae in cadavera showing a postero-inferior open angulation of the anterior urethra.

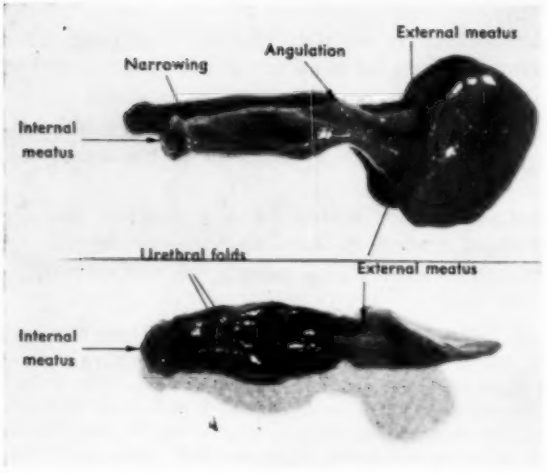


Fig. 4. Cast of a female urethra: Above: = lateral view; Below: = dorsal view.

Results of controls on autopsy material.

1. The narrowing of the posterior urethra was present.
2. Any angulation of the posterior urethra was not found.
3. The middle part of the urethra was the widest portion and had a spool-shaped lumen.
4. The occurrence of narrowing and angulation between the middle and lower thirds of the urethra was established.
5. Immediately proximal to the external meatus, the urethra formed a small potential cavity with a certain resemblance to the fossa navicularis in the male.

Discussion

The course and shape of the female urethra is more complicated than usually believed.

The distension of the middle third during miction, the narrowing and angulation between the middle and lower thirds and the navicular fossa of the anterior urethra may possibly be of importance for an understanding of miction in the female.

It is easy to demonstrate by roentgenologic technique a navicular fossa in the female urethra. It is more difficult to explain its occurrence.

According to present embryologic conceptions, the anterior urethra of the male develops from the same tissues as the labia minora in the female. The appearance of a navicular fossa in both sexes may indicate that this belief is erroneous. It does not appear altogether impossible that the distal part of the female urethra may originate from the same tissue as that of the male; in this case it seems reasonable to explain the occurrence of the navicular fossa in the male as well as in the female as an anatomic detail caused by function.

It is possible that the described narrowings, the angulation and the two widenings of the female urethra may have some function in forming whirls and thereby an increased resistance during miction. A definite perception of normal miction is thus formed. The function would fail in incontinent patients with short, straight urethrae devoid of the anatomic details mentioned.

SUMMARY

By using a new technique for lateral urethrograms during miction it has been possible to demonstrate certain details, not previously described, of the shape and course of the middle and anterior portions of the female urethra. The findings were controlled by studies on autopsy material.

ZUSAMMENFASSUNG

Durch Benutzung einer neuen Technik für laterale Urethrogramme während der Miktion ist es möglich gewesen, gewisse bisher nicht beschriebene Einzelheiten der Form und des Verlaufes des mittleren und vorderen Teiles der weiblichen Urethra zu demonstrieren. Die Befunde wurden durch Studien an Sektionsmaterial kontrolliert.

RÉSUMÉ

L'emploi d'une nouvelle technique d'uréthrographie mictionnelle a permis de mettre en évidence quelques détails de la forme et du cours de l'urèthre moyen et antérieur chez la femme, qui n'avaient pas été décrits auparavant et ont été controlés par quelques examens autopsiques.

REFERENCES

1. Anson, B. J.: Anatomy of the Female Genitalia. Chap. I. Obst. and Gynecol. Edit. by A. H. Curtis. W. B. Saunders Co., Philadelphia 1933.
2. Bonney, V.: On Diurnal Incontinence of Urine in Women. J. Obst. & Gynaec. Brit. Emp. 30 (1923), 358.
3. Broman, I.: Människokroppen, Vol. III. (Swedish.) Lund 1936.
4. Corning, H. K.: Lehrbuch d. Topographischen Anatomie. Verlag v. J. F. Bergmann, München 1923.
5. Counseller, U. S.: Urinary Incontinence in Women. Am. J. Obst. & Gynec. 45 (1943), 479.
6. Curtis, A. H. et al.: The Anatomy of the Pelvic and Urogenital Diaphragms in Relation to Urethrocele and Cystocele. Surg., Gynec. & Obst. 68 (1939), 161.
7. Curtis, A. H.: Textbook of Gynecology. 5th ed. W. B. Saunders Co., Philadelphia 1947.
8. Davies, J. W.: Urinary Stress Incontinence — its Relation to Cystocele and Lacerations of the Pelvic Floor. J. Urol. 48 (1942), 536.
9. Folsom, A. I. and O'Brien, H. A.: The Female Urethra. J. A. M. A. 128 (1945), 408.
10. Goff, B. H.: The Surg. Anatomy of Cystocele and Urethrocele with special Reference to the pubocervical fascia. Surg., Gynec. & Obst. 87 (1948), 725.
11. Gray, H.: Anatomy of the Human Body. Ed. by W. H. Lewis. 23d ed. Lea and Febiger, Philadelphia 1936.
12. Groschuff, K.: Über intraepitheliale Drüsen der Urethraschleimhaut. Anat. Anz. 12 (1896).
13. Ingelman-Sundberg, A.: The Pubovesical Ligament in stress Incontinence. Acta obst. et gynec. Scandinav 28 (1949), 185.
14. Kalischer, O.: Die Urogenitalmuskulatur des Dammes, mit besonderer Berücksichtigung des Harnblasenverschlusses. Verlag S. Kager, Berlin 1900.
15. Krantz, K. E.: The Anatomy of the Urethra and Anterior Vaginal Wall. Am. J. Obst. & Gynec. 2 (1951), 374.
16. Lüdinghausen, H. J. v.: Ztschr. Anat. 97 (1932), 757.
17. Miller, D.: Studies on Cystocele and Urinary Incontinence in the Female by Use of Cystograms and Urethrograms. J. Urol. 40 (1938), 612.
18. Morris' Human Anatomy. Ed. by C. M. Jackson. 9th ed. P. Blakiston's Son and Co., Philadelphia 1933.
19. Möllendorff, W. v.: Handbuch d. Mikroskopischen Anatomie des Menschen. Vol. I. Verlag v. Julius Springer, Berlin 1930.
20. Natvig, H.: Incontinentia urinae hos kvinnen. (Norwegian.) Norsk mag. f. laegevidensk. 92 (1931), 325.
21. Nordenström, B. E. W.: A Method for Topographic Urethrocystography of Women. Acta radiol. 37 (1952), 503.
22. Rauber-Kopsch: Lehrbuch u. Atlas d. Anatomie des Menschen. Vol. III. Verlag v. Georg Thieme, Leipzig 1940.
23. Reddington, M.: Stress Incontinence. Brit. J. Urol. 20 (1948), 77.
24. Sante, L. R.: Manual of Roentgenological Technique. Edwards Bros., Inc., Ann Arbor, Michigan 1944.
25. Schäfer, E. A. and Thane, G. D.: Quain's Anatomy. Longmans Green and Co., London 1896.
26. Stevens, W. E. and Smith, S. P.: Roentgenological Examination of the Female Urethra. J. Urol. (1937), 195.
27. Tomsen, E.: Roentgen Examination of the Female Urethra. Acta radiol. 11 (1930), 527.
28. Tomsen, E.: Studies of the Female Urethra, Especially as Regards the Closing Mechanism of the bladder. Acta radiol. 13 (1932), 433.
29. Zangemeister: Verschluss der weiblichen Blase. Ztschr. für gynäk. Urol. 1 (1909), 79.

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BONE CHANGES IN CASES OF SUPRASELLAR MENINGIOMA

by

Giovanni Di Chiro and *Erik Lindgren*

To a certain extent, meningiomas produce changes which may be observed by ordinary roentgen examination of the skull. They may give rise to the formation of new bone or to bone destruction and if abundantly vascularized. meningiomas cause dilatation of the arterial and venous grooves in the calotte. Basal meningiomas, especially those which grow en plaque, to a very great extent give rise to osteosclerosis which resembles and may be very difficult to distinguish from fibro-osteomas. These types of meningioma occur particularly above the lesser and greater wings of the sphenoid bone. The meningiomas which are usually called suprasellar mengiomas, on the other hand ». . . do not, as a rule, cause the reactive hyperostosis that so often makes it possible to determine the exact point of origin of meningiomas elsewhere in the cranial chamber». This quotation from CUSHING and EISENHARDT is probably in conformity with the common conception. Isolated cases are described, however, in which bone changes have been noted. Thus, in one case, LYSHOLM and OLIVECRONA described a thickening in the region of the tuberculum sellae — the point of origin, according to CUSHING, of suprasellar meningiomas. Changes of the same kind have also been reported by HOLMES (1 case), CUSHING and EISENHARDT (1 case) and DAVIDOFF and EPSTEIN (2 cases).

It would therefore appear from the literature that the suprasellar meningiomas only rarely cause bone changes. Such is in our experience, however, not the case. This is probably because the bone changes which occur are difficult to observe and the normal anatomy of this region, as seen roentgenographically, is not properly appreciated. The formations which are important in this connection are the thickness of the planum

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sphenoidale and the size and shape of the limbus sphenoidalis, the tuberculum sellae and the sulcus of the optic chiasm between them. A schematic sketch showing the appearance of the different anatomical variations of these parts in a true lateral view of the skull may be seen in fig. 1. We have not made a statistical analysis of a large material and the figures mentioned below are thus only approximative. They give, however, an idea of the relative frequency of these variations. The most usual appearance is shown in fig. 1 a. The sulcus of the chiasm

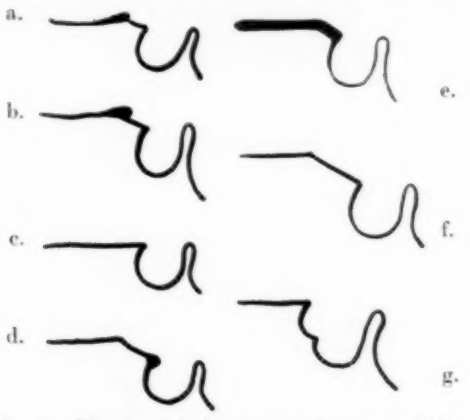


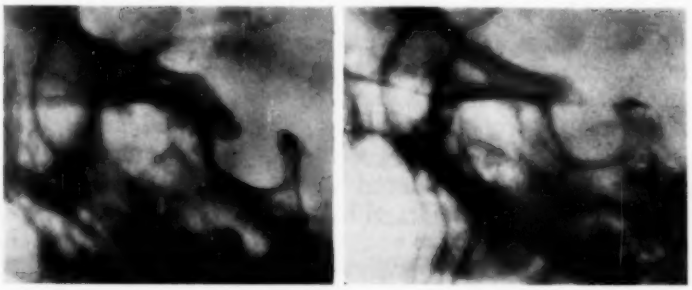
Fig. 1. Diagram of the most common variations in the presellar region.

does not actually merit the denomination sulcus in these cases but appears rather as a straight line, generally between four and eight millimeters in length. There is no recognizable thickening of the bone of the tuberculum sellae, but the limbus sphenoidalis is prominent and appears as a thickening at the anterior border of the sulcus of the chiasm. In a material of 100 cases, this condition was found in 71; in 10 cases, the limbus sphenoidalis was particularly thick and knob-like (fig. 1 b, 2 a). Almost as often, however, no clear border between the planum sphenoidale and the sulcus of the chiasm was found; these lie in the same plane and the bone, seen in the lateral view, has an even thickness of about one millimeter. This was apparent in eight cases of this series (fig. 1 c, 2 b). Other anatomic variations are relatively rare; one such variation consists of an increase in size of the tuberculum sellae, which presents a knob-like appearance. This occurred in five cases (fig. 1 d). In certain cases, the planum sphenoidale and the sulcus of the chiasm are particularly thick, up to two millimeters, but the bone is sharply defined and its structure homogeneous (three cases in 100; fig. 1 e). In two cases, the

sulcus of the chiasm was especially long, one centimeter or more (fig. 1 f). In rare cases, the sulcus may be markedly concave upwards (fig. 1 g). The sellar region as seen laterally in such cases presents what has been described as an »omega-shape», »J-shape», or »hour-glass-shape»; this is said to be characteristic of a glioma of the optic chiasm.

We have reviewed the plain roentgenograms of 45 cases of verified meningioma. Of these, 22 showed the appearances in the immediate presellar region to be quite normal but in not less than 23 cases — *i. e.*, about 50 per cent — definite pathologic changes were seen. This is a figure which in no way agrees with that given in the literature. In these 23 cases, there was a bone change anterior to the sella, consisting of a thickening of the planum sphenoidale immediately in front of the limbus sphenoidalis. The degree of thickening varied and usually measured as much as four to six millimeters; in certain cases, a true bonemound up to almost a centimeter in height could be observed. Occasionally, the entire region from the tuberculum sellae to the anterior border of the planum sphenoidale was involved and in certain cases the change also extended over the most posterior part of the plate of the ethmoid bone. The bone structure in the region of the change was always pathologically changed. This is of vital importance in the differential diagnosis between the normal variation shown in fig. 1 e, and a change caused by a meningioma. The density of the bone tissue in this region may approximate, of course, to the normal but the structure is always more or less irregular and the surface is not evenly or sharply defined as in normal cases.

That which is clinically designated as a suprasellar meningioma is reported, as a rule, as originating from the tuberculum sellae. This receives no direct support from the present investigation, inasmuch as the bone changes in every case are essentially localized to the tract of the limbus sphenoidalis and only extend backwards as far as the tuberculum sellae in certain cases. A survey of 30 verified mengiomas, which, from the clinical signs were characterized as being olfactory groove meningiomas, shows that seven presented the same bone changes previously mentioned — localized to the planum sphenoidale; similar thickening of bone was never found in the olfactory groove — pressure atrophy only was seen. From this material, it is impossible to draw any conclusions as to whether the meningiomas in these seven cases, which clinically gave the impression of being olfactory groove meningiomas but presented the same bone changes as those designated as meningiomas arising from the tuberculum sellae, originated above the planum sphenoidale and subsequently grew anteriorly. This, to us, appears to be the most probable explanation.



a. b.

Fig. 2. a. Normal case. The limbus sphenoidalis knob-like.
b. No clear border between the planum sphenoidale and sulcus chiasmatis.

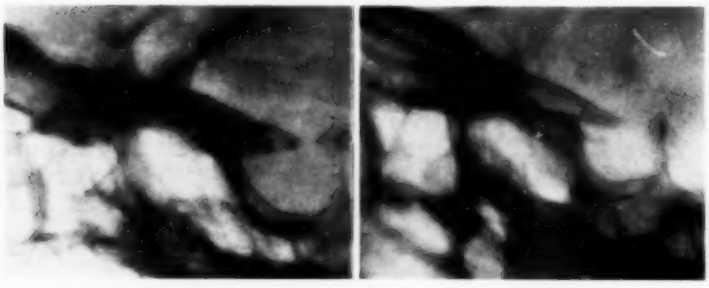


Fig. 3. Fig. 4.

Fig. 3. Suprasellar meningioma. The entire region from the tuberculum sellae to the anterior border of the planum sphenoidale is thickened, with pathologic bone structure.

Fig. 4. Suprasellar meningioma. Small hyperostosis. The planum sphenoidale and the limbus sphenoidalis are involved. No change in the sulcus chiasmatis or tuberculum sellae.

The bone changes caused by suprasellar meningiomas appear most clearly in the lateral view of the skull but may be observed more or less distinctly on P. A. or A. P. roentgenograms taken with a beam projection parallel to the planum sphenoidale. Ordinary skull roentgenograms, taken with sufficient penetration and with the patient positioned exactly, are required. Tomography is not at all necessary to demonstrate the changes although it may be of value in doubtful cases. As regards the shape of the sella turcica in these 45 cases: in 9, there were definite sellar changes

Fig. 5.

Fig. 6.

Fig. 5. Suprasellar meningioma. Hyperostosis of the sulcus chiasmatis gradually decreasing anteriorly but the whole planum sphenoidale is involved.

Fig. 6. Clinically, olfactory groove meningioma. Large hyperostosis involving the whole planum sphenoidale backwards to the limbus sphenoidalis (Cf. fig. 4).

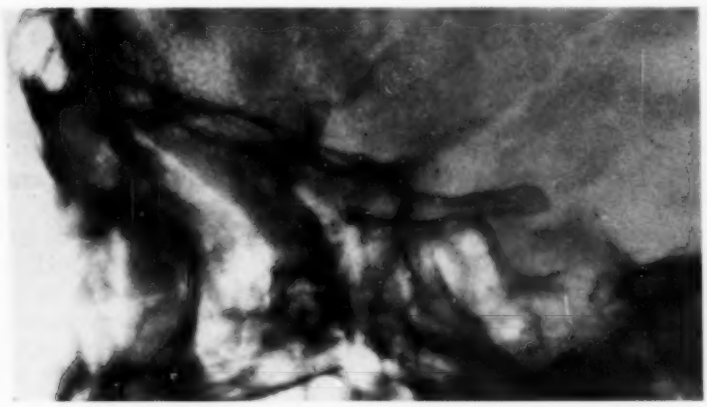


Fig. 7. Usual roentgenologic changes in olfactory groove meningiomas. No change in the planum sphenoidale. Pressure atrophy in the anterior part of the floor of the anterior cerebral fossa.

in the form of enlargement with more or less marked destruction of the floor and the dorsum; in 25, the sella was normal; and in the remainder, the sella showed no definite changes although the dorsum was unusually short. Thus, this agreed with the general conception; *i. e.*, a comparatively low incidence of sellar changes exists in cases of suprasellar meningioma. In three cases, the meningioma was calcified.

SUMMARY

After a schematic review of the normal variations in the presellar region, a report is given of bone changes occurring in 23 out of a material of 45 cases of suprasellar meningioma.

ZUSAMMENFASSUNG

Nach einer schematischen Übersicht über die normalen Variationen der präsellären Gegend werden Skelettveränderungen in 23 von 45 Fällen mit suprasellären Meningeomen berichtet.

RÉSUMÉ

Les auteurs rapellent schématiquement les variations normales de la région présellaire; ils ont trouvé des lésions osseuses dans 23 cas de méningiome suprasellaire sur 45.

REFERENCES

1) Cushing, H., and Eisenhardt, L.: Meningiomas arising from the tuberculum sellae with the syndrome of primary optic atrophy and bitemporal field defects combined with a normal sella turcica in a middle-aged person. Arch. Ophth. 1 (1929), 1 and 168.
2) Davidoff, L. M., and Epstein, B. S.: The abnormal pneumoencephalogram, p. 156. Lea and Febiger, Philadelphia 1950.
3) Holmes, G.: Suprasellar tumours. Tr. XIII Concilium Ophthalmologicum, Hollandia, 3 (1929), 65.
4) Olivecrona, H., and Lysholm, E.: Die chirurgische Behandlung der Gehirntumoren. Springer Verlag, Berlin 1927.

FROM THE RADIATION PHYSICS DEPARTMENT, UNIVERSITY OF LUND (DIRECTOR: K. LIDÉN), AND KING GUSTAV V'S JUBILEE CLINIC (DIRECTOR: B. EBENIUS), LUND, SWEDEN

A 10-CURIE Co^{60} TELEGAMMA UNIT

(Preliminary report)

by

Kurt Lidén

The present paper briefly reports the initial performance and measurements of a new Co^{60} telegamma unit at King Gustav V's Jubilee Clinic, Lund. This unit has been in use for clinical treatment since December 1951. Full details will be published elsewhere at a later date.

It was decided in 1949 to increase substantially the stock of radium needles for clinical treatments. At the same time information from the Isotope Division, A. E. R. E., Harwell, England, gave reason to believe that Co^{60} in amounts sufficiently large for use in telegamma units would become available during 1950. It appeared possible to take advantage of the availability of Co^{60} by redistributing the Ra of the existing telegamma unit in Ra needles and using Co^{60} in the telegamma unit in its place. The employment of Co^{60} would at the same time make it possible to utilize greater quantities of radioactive material, and indeed clinical experience with the 2 gr Ra unit had shown that this would be very desirable; 10 curies of Co^{60} were therefore ordered from Harwell in the spring of 1950.

The cobalt, in two large concrete drums, arrived in Lund in January 1951, and the complete apparatus was set up in Nov. 1951. The design is fundamentally the same as previously (1, 2) but the lead shielding has been increased from 10 to 12.5 cm. The dimensions and the focal—skin distance (*F. S. D.*) of the new nozzles have also been increased.

»Hot» work began on December 3rd. The two bulks of cobalt, each containing 8 cylindrical 6 × 6 mm pieces with an activity of 600 mc were transferred with remote-control tools through the window of the telegamma room from the concrete drums to a lead- and iron-shielded box situated just below the telegamma apparatus. From this position,

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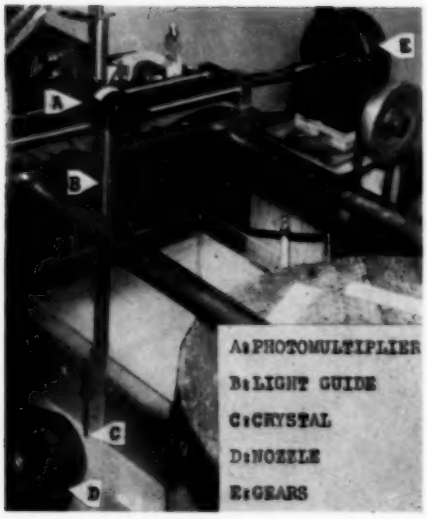

Fig. 1. The detector element of the radiation measuring equipment used in intensity distribution measurements of the Co^{60} telegamma unit.

the Co^{60} sources were mounted in small aluminium containers. Special remote-control tools, bent at right-angles, were used for this purpose and the procedure was watched in mirrors. The activity of each source was measured before loading the container of the telegamma apparatus.

The intensity distribution of the new unit in a $30 \times 30 \times 25$ cm water phantom was investigated. A scintillation detector, consisting of a $3 \times 3 \times 3$ mm terphenyl crystal, a perspex light guide and a photomultiplier, served as radiation detector (Fig. 1). The tube current was continuously registered on a 6 mV Speedomax recorder, while the remote controlled motor-driven detector moved with constant velocity along equidistant lines parallel with the central axis of the beam (Fig. 1). The surface dosage rate was extrapolated from measurements by means of small ion-chambers. Both the detector and the ion-chambers were calibrated with Ra sources.

The *F. S. D.* of the nozzle now used is 6.5 cm and the area of the circular field is 28 cm². In December 1951 the surface dosage rate of the water phantom was 39.3 r/hour. The Co^{60} activity was 8.9 curies. The surface dosage rate in air, calculated on the assumption that 1 curie of Co^{60} gives 225.5 r/min. at a distance of 1 cm, is 42.4 r/min.

The percentage depth doses along the central axis for the new Co^{60} — and the old Ra-unit are shown diagramatically in Fig. 2. The upper curve in Fig. 2 gives the ratio of the percentage depth doses (D_d) of the Co^{60} and the Ra units, the latter recalculated for 6.5 cm *F. S. D.* (3). This curve has also been checked from depth dose measurements with ion-chambers. The shape of the curve must be a consequence of the different γ-ray spectra of Co^{60} (1.17 and 1.33 MeV) and Ra (12 strong lines 0.2 — 2.2 MeV).

Exposure of the personnel to radiation during the mounting procedure was continuously measured with suitable ion-chambers and by the film-badge method. The intensity distribution near the lead con-

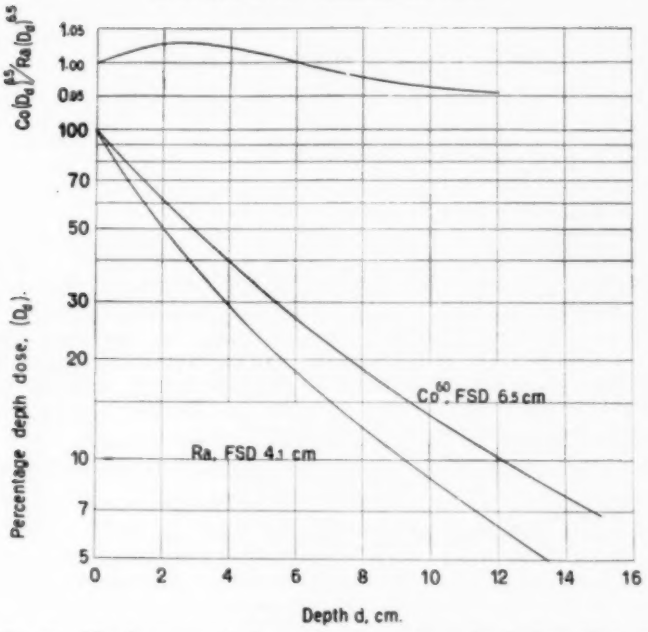

Fig. 2. The lower part shows the percentage depth dose (D_d) of the Co^{60}-unit, *F. S. D.* 6.5 cm, and of the Ra-unit, *F. S. D.* 4.1 cm. Field area in both cases, 28 cm^2. The upper part: the depth dose ratios Co $(D_d)^{6.5}$/Ra $(D_d)^{6.5}$. The calculation of the Ra (D_d) values for *F. S. D.* 6.5 cm are based on the measured (D_d) values for *F. S. D.* 4.1 cm.

tainer of the unit was also carefully studied. The intensity on the surface of the container was found to be 50—100 mr/hour but at 50 cm from the latter it was only 10—15 mr/hour. Investigation of the scattered radiation in the neighbouring rooms when the unit was in operation showed only negligible values.

The unit has now been used for clinical treatment for three months. The short treatment times have proved to be most advantageous although the increased nozzle dimensions sometimes present difficulties. Finally, clinical experience seems to indicate that for equal skin doses, skin reactions following Co^{60} irradiation are milder than those after Ra irradiation.

The object of the work in progress at the time of writing is to measure the intensity distribution when the beam head is fitted with 10 cm *F. S. D.* nozzles for circular and rectangular fields.

SUMMARY

A 10-curie Co^{60} telegamma unit *F. S. D.* 6.5 cm is now in operation at King Gustaf V's Jubilee Clinic, Lund. The mounting of the Co^{60} sources is briefly described. Depth doses measured in a water phantom show only small differences from those of Ra, at the same *F. S. D.*

Clinical experience of the treatment seems to indicate that the skin reaction to Co^{60} irradiation is milder than to an equivalent Ra dose.

ZUSAMMENFASSUNG

Eine 10-Curie Co^{60}-Telegamma Apparatur mit einem Fokus-Haut-Abstand (*F. H. A.*) von 6.5 cm ist in Lund in Gebrauch genommen worden. Die Montierung der Kobaltpräparate wird beschrieben. Tiefendosismessungen mit einem Wasserphantom zeigen, dass die Tiefenwirkung von Co^{60} und Ra bei gleichem F. H. A. ungefähr dieselbe ist.

Klinisch scheint nach den bisherigen Erfahrungen die Hautbelastung geringer als für die gleiche Radiumdosis zu sein.

RÉSUMÉ

Un appareil de télégammathérapie chargé de 10 Curies de Co^{60} avec une distance focale de 6.5 cm est actuellement en fonctionnement à la clinique du Jubilée du Roi Gustave V, à Lund. La mise en place du Co^{60} est décrite. Les mesures de doses en profondeur dans un fantôme d'eau montrent par rapport au Ra, une difference petite en profondeur pour la même distance focale.

L'expérimentation clinique du traitement semble montrer que la réaction cutanée à l'irradiation par le Co^{60} est moins forte que pour une dose équivalente de Ra.

REFERENCES

1. Benner, S.: A new teleradium apparatus. Acta radiol. 28 (1947), 765.
2. Lidén, K.: The intensity distribution of the 2 gr teleradium unit of the King Gustaf V's Jubilee Clinic in Lund. Acta radiol. 30 (1948), 76.
3. Mayneord, W. V. and Lamerton, L. F.: A survey of depth dose data. Brit. J. Radiol. 14 (1941), 255.

FROM RADIUMHEMMET (DIRECTOR: PROFESSOR H. AHLBOM), STOCKHOLM, SWEDEN

TELERADIUM TREATMENT OF LARYNGEAL CARCINOMA AT RADIUMHEMMET, STOCKHOLM

by

Folke Jacobsson

Up to the 1920s the treatment of laryngeal carcinoma was purely surgical. At that period operation, if at all possible, was in most cases synonymous with laryngectomy. A communication then came from COUTARD to the effect that he had succeeded in curing a few cases of carcinoma of the larynx by roentgen therapy.

Coutard's method or a modified version was gradually adopted. Other cases of cures of cancer of the larynx by radiotherapy were soon reported. In 1932, COUTARD described several more successes with his method. It was now also seriously discussed whether irradiation in certain cases could not take the place of operation.

Extensive statistics have gradually been produced both from laryngologic and radiotherapeutic sources. As a whole it may be said that discussions up to now have resulted in more or less firm agreement that those cases that can be operated on by laryngo-fissure and excision of the tumour are also suitable for fractional irradiation. The results appear to be the same with both methods.

It is very different in those cases in which the tumour is too widespread for laryngo-fissure and excision and in which only laryngectomy presents a prospect of radical removal of the tumour. This is where opinions differ when the value of irradiation is discussed.

Laryngeal cancer mainly affects men and usually at their most active age. The records of Radiumhemmet show that a fraction more than every fifth male patient is under 50 years of age. Laryngectomy means for many of these men, unable to follow their previous occupations, a social and economic handicap. It would therefore be of great importance if certain types of cancer of the larynx could be selectively treated with

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the assurance that irradiation would give equally good chances of permanent cure as laryngectomy.

Classification

The term »cancer of the larynx» has not exactly the same meaning at different clinics. At Radiumhemmet and many other clinics however, the borderline between the larynx and the hypopharynx has been drawn at the laryngeal inlet. The tumours around the inlet are hard to group, as in many cases it is difficult to decide on which side of the inlet the tumour has arisen.

Our records have also been divided into groups according to the situation and extension of the tumours in the larynx. This classification, which in the main is the same as the one previously used by FRENCKNER and AHLBOM, takes into consideration the suitability of cases for various surgical procedures.

Group I: The tumour is limited to one vocal cord. Anteriorly, it does not extend to the anterior commissure or posteriorly to the processus vocalis. The mobility of the vocal cord is unimpaired. (In some early cases the tumour may be removed endolaryngeally or by laryngotomy and excision.)

Group II: Cancer confined to the vocal cords; not extending posteriorly to the processus vocalis but spreading from one vocal cord over the anterior commissure and also involving larger or smaller portions of the anterior part of the other vocal cord. The mobility of both vocal cords is unimpaired or slightly restricted. (The growth may be removed by extended laryngo-fissure, an operation which may often be followed by certain disturbances of the function of speech.)

Group III: More widespread, unilateral laryngeal cancer. The growth infiltrates neither the anterior commissure nor, to any degree, the aryregion. The mobility of the vocal cord is restricted or absent. (In certain cases the growth may be removed by hemilaryngectomy, otherwise only total laryngectomy is possible.)

Group IV: Widespread uni- or bi-lateral cancer of the larynx. All cases with regional lymph gland metastases are classed among this group. (In operable cases, only laryngectomy can be considered.)

Clinical Material

178 cases of larynx cancer have been treated during the period 1935—1945. 7 more cases were examined in the same period but were too far advanced and were therefore not accepted for treatment.

The distribution of cases during the different years of the treatment period is shown in *Table I*.

Table I

Distribution of patients in the different years

Year	Accepted	Not accepted
1935	9	2
1936	9	0
1937	10	0
1938	15	0
1939	17	0
1940	15	2
1941	20	0
1942	24	2
1943	19	1
1944	22	0
1945	18	0

The composition of the material according to distribution in groups is shown in *Table II*.

Table II

Distribution according to groups

Group I	20 cases (11 per cent)
Group II	12 cases (7 per cent)
Group III	39 cases (22 per cent)
Group IV	107 cases (60 per cent)

As shown in Table II the main portion of the cases belong to Group IV. Within this group, the tumour had grown through the larynx and infiltrated the surrounding tissues in 47 cases.

Age distribution

Reports on the distribution of cancer of the larynx within various age groups are fairly consistent. MARTIN states that 2 % of his patients were under 40, and 47 % were over 60 years of age. The youngest patient was 26. In OESER's report (1943) 5 % of all cases were under 40. MUSTAKALLIO (1944) reports his youngest patient as being 35 and the average age, 54.

The distribution within the various age groups in our records is shown in *Table III*.

Table III

Distribution according to age

Age	Men	Women
20—29 years	—	3
30—39 »	6	—
40—49 »	24	5
50—59 »	53	5
60—69 »	57	6
70—79 »	13	2
80— »	4	—

From *Table III* it will be seen that 5 % of the patients were under 40 years of age, 16 % were between 40—49, 33 % between 50—59, and 46 % were 60 years old or over.

Moreover, 38 patients or 21 % were under 50 and consequently in their most productive age.

It is remarkable that there are 7 relatively young patients in the records, one being 20, two 23, one 30 and three 31 years of age. As a matter of interest it is worth mentioning that five of these were admitted for treatment during the same year (1942).

The youngest patient was 20 and a woman. The oldest was a man of 84.

Sex distribution

For a long time it has been generally known that cancer of the larynx mainly occurs in men. In Sweden, however, there are proportionally rather more women with cancer of the larynx than in other countries. The cause of this is the relatively common occurrence of sideropenia or Plummer-Vinson's disease in Sweden. This disease occurs almost entirely in women and predisposes to cancer. It is, however, of little importance as a predisposing factor in cancer of the larynx compared with its influence, for example, in hypopharyngeal cancer (AHLBOM and JACOBSSON).

In *Table IV*, I have collected information in sex distribution from a few representative foreign records.

Table IV.

Sex distribution

Country	Total No. of cases	Percent of men
England (WINDEYER 1947)	106	96
Finland (MUSTAKALLIO 1944)	201	99
France (BACLESSE 1950)	341	96
Germany (OESER 1943)	468	93
Sweden (JACOBSSON 1951)	178	88
U. S. A. (New York) (MARTIN 1947)	362	98
U. S. A. (California) (LOW-BEER 1950)	157	90

Predisposing Factors

Most authors consider regular smoking to be a predisposing factor in laryngeal cancer and especially in cancer of the vocal cords. It is less agreed as to the importance which should be attached to vocal strain. Some authors have also tried to prove that occupation plays its part, particularly in those exposed to dust and irritating chemical fumes.

Smoking

MUSTAKALLIO (1944) has examined his records in an attempt to prove the importance of smoking. Of 167 patients with cancer of the larynx questioned, 165 (98 %) were smokers and about 45 % of these were heavy smokers. Two of the patients commenced to smoke regularly at the age of 4, and twelve at the age of 10. On an average the patients started smoking at the age of 18. Examining other records for control he found that only 78 % of the patients questioned were smokers and that these on an average started smoking at as late an age as 31.

MARTIN (1947) found that 97 % male and 50 % female patients were smokers. Examining other records for control he found the figures to be 89 % for male and 20 % for female patients. Among patients with cancer of the larynx 70 % were heavy smokers against only 55 % in the control records.

AHLBOM, who examined previous cases of cancer of the larynx at Radiumhemmet, found that a considerable number of the patients were heavy smokers.

In the present material there are figures for smoking in 111 of the male and in 5 of the female cases. Of the males, 107 (96 %) were smokers and of these no fewer than 63 % were heavy smokers. It is remarkable that many declared that they had been smokers since childhood. There was only one female smoker and she smoked a pipe.

Our impression at Radiumhemmet is that it is lengthy, intensive smoking that is important as a cancer-predisposing element especially if the patient is also in the habit of inhaling.

Vocal strain and occupation

It has previously been noticed that certain occupations often occur unproportionally among patients with cancer of the larynx. In England, according to WILLIS, it is clear from the Registrar-General's Report of 1931 that fatal carcinoma of the larynx showed a decided class gradient among males, being highest in the unskilled classes; laryngeal cancer however, showed no class gradient in women, suggesting that the factors responsible for the excess of cancer at this site among unskilled males are directly associated with occupation.

MUSTAKALLIO (1944) has been thinking along the same lines and has found that about 90 % of his patients belonged to the unskilled classes.

When checking our records it was remarkable to find that there were so many carpenters and painters. They form together 8 % of all the patients. On account of this I have made an approximate estimation of the number of patients who followed a sooty or dusty occupation, the

number exposed to irritating chemical fumes while at work, and the number who ran the risk of vocal strain. Finally, in another group I have collected those patients who, through their occupation, were much out-of-doors, and could therefore be considered specially disposed to laryngitis (sailors, policemen etc.).

In *Table V* is shown the approximate distribution of the different groups.

Table V

Distribution according to occupational risk

I.	Soot or dust	30 per cent
II.	Chemically irritating fumes	10 per cent
III.	Vocal strain	35 per cent
IV.	Outdoors	15 per cent
V.	Other occupations	10 per cent

MARTIN has discussed the importance of vocal strain as predisposing to cancer of the larynx; he was able to follow changes in the larynx in two patients (a soldier and a huckster) who were liable to such strain. After three years' control both these patients developed cancer of the vocal cords. In one of our patients, a woman teacher, cancer developed five years after the presence of laryngitis had been established; this defied treatment and incapacitated the patient for work.

If, to the irritation to which the larynx is exposed by a particular occupation is added the effect of intensive and assiduous smoking, it is not so unnatural that sensitive subjects may develop cancer of the larynx.

Duration

Carcinoma of the larynx, especially of the vocal cords, has often a slow course. In its early stages it causes little trouble and then usually in the form of undefinable hoarseness. It is, therefore, often some time before the patient sees a doctor; there may be a history of hoarseness of one or several years' duration.

In our records we find statements on the duration in 166 cases. The figures of the duration of the cases and their distribution in various groups are shown in *Table VI*.

Table VI

Duration in the various groups.

Duration in months	Group I	II	III	IV
0—2	6	2	3	4
2—4	4	4	8	25
4—6	3	2	8	10
≧ 6	6	2	19	60

In 52 % of the cases the patients stated that they had suffered from symptoms for half a year or even longer.

Site of Primary Tumor

A great number of the cases were too far advanced to make it possible to decide the site of the origin of the tumour in the larynx. However, some idea of the nature of the material is given by recording as far as possible the starting-point of the growth.

The cases have been grouped according to site of origin in *Table VII*.

Table VII

Site of origin of primary tumour.

Vocal cord	71	cases
False cord	4	»
Ventricle	2	»
Subglottis	5	»
Epiglottis	7	»
Ary-epiglottic fold	1	»
Ary region	2	»
Impossible to decide the site of origin of the tumour owing to tumour-spread	86	»

Metastases

In this present material no metastases of the lymphatic glands have been noticed in pure cancers of the vocal cords. BACLESSE has the same experience. According to JACKSON (1939) the cause of this is: »In the elastic tissue of the vocal cords themselves, lymphatics are practically absent and they are few in the connective tissue of the cords.» On the other hand tumours above the glottis and in the subglottis metastasise fairly early. It is usually said that the further from the glottis and nearer the sinus piriformis the tumour is situated, the more early and readily will it form metastases.

The frequency of metastases of the lymphatic glands therefore varies with different materials depending upon the varying proportions of cancer of the vestibulum and of the subglottis. In our material metastases of the lymphatic glands were observed in 37 cases (20 %) and in 7 of these there were also distant metastases.

The frequency of metastases of the lymphatic glands in published material is between 10—20 %. ACKERMAN and REGATO give the frequency as 10 % and TAYLOR and NATHANSON as 18 %. BACLESSE (1949) in his large material of more than 300 cases found metastases of the lymphatic glands in 16 %.

Histology

All cases in the material consist of squamous cell carcinoma. In 15 cases the microscopic examination showed a low-differentiated squamous cell carcinoma. All these cases belonged to Group IV and were thus as expected advanced cases.

Methods of Treatment

Carcinoma of the larynx is treated operatively, by roentgen or radium or by operation + post-op. irradiation. Pre-operative irradiation is practically never carried out. Some authors consider that a trial with irradiation may be made in all cases without risk. Should this not succeed they consider operation later on always possible. MARTIN warns against such test irradiation treatment and points out that in spite of careful controls, an operable case can become inoperable during irradiation either through continued growth of the primary tumour or by reason of metastases.

Roentgen treatment of carcinoma of the larynx is usually spread over 4—6 weeks. Treatment over a longer period is given for example by BACLESSE and REGATO, who often extend its administration over 6—10 weeks. In Chicago COUTARD (1940) began to use concentrated roentgen treatment for cancer of the larynx and this method has been continued by CUTLER. The latter has used 400 kv radiation and has usually given treatment for 18 days with tumour-doses of 6,000—6,500 r; otherwise, tumour-doses of between 5,000—8,000 r depending upon the duration of the treatment, have been administered.

Cancer of the vocal cords has, especially in suitable cases in England, been treated according to the FINZI-HARMER fenestration method by the application of radium needles (CADE and PATERSON).

Teleradium treatment has, except at Radiumhemmet, been used to a certain extent only at a few clinics (CADE, LEDERMAN, WINDEYER) and the treatment has usually been divided up as in roentgen treatment.

As regards the treatment of the metastases of the lymphatic glands, neck dissection is normally advised. However, for secondaries from tumours of the epiglottis and the false cords, irradiation alone is often given, as these metastases are usually radio-sensitive.

Treatment at Radiumhemmet

When a case is received for treatment consideration is first given to the extent and macroscopic appearance of the tumour as well as to the mobility of the vocal cords by indirect laryngoscopy. The examination is normally supplemented by tomography and also in most cases by direct laryngoscopy primarily to obtain an idea of the condition of the

sinus Morgagni and the subglottis. When these examinations and the pathological findings are completed, the case is discussed with our laryngologists and the most suitable treatment decided upon.

If the case is suitable for radiation therapy, this is as a rule given in form of teleradium treatment. The latter is also given post-operatively in cases surgically treated.

Teleradium treatment is carried out by an apparatus containing 5 g radium and has been described by SIEVERT. The filtration is about equivalent to 6 mm lead and the distance between the radium and the skin is 6 cm. We use circular treatment fields having a diameter of 5 cm. In general three treatment fields are used, one on each side of the larynx and one in front. For more advanced cases and in which there are metastases of the lymphatic glands, the teleradium treatment has to be given to four or five fields. By equal distribution of the dose the distance between the centres of two adjacent fields is 6—6.5 cm. One field is treated daily and by a skin-dose of about 1,000 r.[1]

The treatment is given over a period of between 12—19 days and the tumour-dose has generally been between 6,000—6,500 r.

The mucous membrane reacts to these doses with a moderate degree of epitelite about two weeks after the beginning of the treatment. 1—2 weeks later the skin reacts with a dry epidermitis, which in the centre of the areas often becomes a moderately moist dermatitis.

In the early cases of the material total skin-doses of more than 5,000 r on each side field were often given, but in recent years the dose has been about 4,500 r. For the anterior field the dose has varied between 4,000 —4,500 r.

Necrosis of the skin has not developed in any case. Even after fairly heavy irradiation the skin after 10 years has remained soft, supple and raisable. A moderate degree of telangiectasis can be seen as a permanent change after the treatment.

The patients have been able to stand this concentrated teleradium treatment amazingly well. Patients living in the neighbourhood of Radiumhemmet have generally been treated as out-patients during the whole of the period. Two months after the beginning of treatment many of the purely teleradium-treated patients have been cured and free from symptoms and have been able to take up their normal work again.

Post-operative teleradium-treatment following laryngectomy has generally been given through two fields on each side of the neck. Each area has been given a total skin-dose of between 3,000 and 4,000 r.

[1] One Imc-hour has been calculated to equal 7.5 r. Most workers in other countries, however, now seem to use a value of 8.3. If the latter figure is used, the teleradium doses in this communication will be about 10 % higher.

Metastases in the lymphatic glands have in some cases been operated on primarily after which post-operative irradiation has been given. In most cases of metastases in the lymphatic glands however, the primary tumour and/or the metastases have been inoperable, for which reason the metastases only have been irradiated.

Results of treatment

In the literature the results are usually given either for cases only irradiated or for cases treated by operation only. However, one cannot obtain a clear apprehension of the prognosis in laryngeal carcinoma if a material does not contain cases treated both operatively and radiologically. Some cases have still to be operated on if the patient's life is to be saved, while others may now be treated by irradiation alone.

Statements on the number of cases cured by radiotherapy vary and depend upon the type of case that has been treated. BACLESSE (1950) has reported a five-year cure in 37 % of a material of 132 cases treated by irradiation from 1939 to 1945. The material comprised only primary cases; cases of recurrence after operation, that had been treated, were not included in the results. NIELSEN (1950) treated 1931—1942 115 cases by roentgen and obtained a five-year cure in 47 %.

CUTLER (1950) has treated 98 cases of advanced laryngeal carcinoma with fixed vocal cord by roentgen and obtained a five-year cure in about 18 %.

LENZ (1947) of New York reports a five-year cure of 27 % in 128 cases of laryngeal carcinoma treated by radiotherapy between 1931 and 1941.

LEDERMAN (cit. CADE) treated 17 early cases by teleradium and 12 of these survived 5 years.

The claims of five-year cures after laryngectomy alone also vary and this depends to a very great extent on the fact that the indications for the operation are very different. If it also be performed in early cases a high rate of cure is naturally obtained. NEW, FIGI and others (1947) report from the Mayo Clinic a five-year cure in 60 % of those laryngectomy cases which could be followed; the mortality after operation was given as 1.9 %.

MARTIN (1947) at the Memorial Hospital has stated that in 44 cases treated by laryngectomy from 1937 to 1941, he obtained a five-year cure in 21 (about 47 %).

In this present material from Radiumhemmet all cases have been treated by radiotherapy but in a number of cases operation has been the primary procedure and irradiation carried out postoperatively. By also including such cases in the series, a fairly good idea can be obtained of the prognosis in cancer of the larynx.

Only cases with definite microscopical verification of cancer have been included and the results are based on all cases treated. Every case has been followed for at least five years or until the patient's death; the result is known in all cases.

In 106 cases the tumour has primarily been treated by radiotherapy and in the further 72 cases the patient has both been operated on and received post-operative irradiation.

In all the cases a five-year cure of 51 % has been obtained. If those cases who died from intercurrent disease before the end of the five-year period, free from symptoms of laryngeal carcinoma, are deducted, *a net five-year cure of 57 % is obtained.*

Table VIII shows the figures of cure in the different groups.

Table VIII

Results of treatment of all cases.

Group I:	20 cases treated.	14 five-year cures.	5 patients died from intercurrent disease.
Group II:	12 cases treated.	9 five-year cures.	3 patients died from intercurrent disease.
Group III:	39 cases treated.	27 five-year cures.	6 patients died from intercurrent disease.
Group IV:	107 cases treated.	41 five-year cures.	6 patients died from intercurrent disease.

The results in those cases treated exclusively by irradiation and their distribution in the various groups are shown in *Table IX.*

Table IX

Results of treatment in cases irradiated only.

Group I:	15 cases treated.	12 five-year cures.	1 patient died from intercurrent disease.
Group II:	9 cases treated.	7 five-year cures.	2 patients died from intercurrent disease.
Group III:	27 cases treated.	13 five-year cures.	6 patients died from intercurrent disease.
Group IV:	55 cases treated.	10 five-year cures.	3 patients died from intercurrent disease.

In Table IX those cases in which a recurrence occurred after radiotherapy but in which, however, freedom from symptoms and a five-year cure was obtained by reason of a second operation, have been counted as dead from cancer. On the other hand, these are naturally reckoned as five-year cures in Table VIII. *One thus obtains by radiotherapy alone a five-year cure in 42 cases out of 106 treated (about 40 %). A net five-year cure rate of about 44 % is obtained.*

The results in those cases primarily operated on and post-operatively treated by irradiation are shown in *Table X*.

Table X

Results of treatment in primarily operated and post-operatively irradiated cases

Group I:	5 cases treated.	2 five-year cures.	3 patients died from intercurrent disease.
Group II:	3 cases treated.	2 five-year cures.	1 patient died from intercurrent disease.
Group III:	12 cases treated.	11 five-year cures.	
Group IV:	52 cases treated.	30 five-year cures.	3 patients died from intercurrent disease.

The results in Table X are naturally not directly comparable with those obtained by irradiation alone. Among the only irradiated cases are included all the inoperable cases.

If one examines the results in those cases in which primary laryngectomy was performed and in which postoperative radiotherapy was carried out (62 cases), one finds that 40 became five-year cures (64 %). In another 3 cases the patient remained free from symptoms but died from intercurrent disease.

Factors Influencing the Prognosis

A. Extension of primary tumour.

In cases of cancer of the vocal cord (Groups I and II), primary freedom from symptoms was obtained in all cases after teleradium treatment. In 19 out of 24 cases a five-year cure was obtained. Of the other 5 cases 3 died from intercurrent disease. One case (inoperable owing to age) recurred after 1 year owing to too small a tumour-dose; it received further teleradium treatment and died from necrosis 2 years after the beginning of treatment. In the remaining case a recurrence following the irradiation occurred 1 $^3/_4$ years later, owing to too small a tumour-dose. After operation the patient became free from symptoms again and eventually died from intercurrent disease.

When the tumour of the vocal cord commences to infiltrate the surrounding tissues the conditions become different. These cases are usually too widespread to afford a chance of radically removing the tumour only by laryngotomy plus excision. One can then choose between laryngectomy subsequently combined with irradiation and the latter alone.

LENZ recommends radiotherapy in all cases of cancer of the vocal cord with the exception of those with subglottis extension or involvement of the arytenoid. CADE states that in cases in which the lesion has

extended beyond the cord, permanent arrest of the disease has not been obtained except in a very small proportion of cases (by teleradium).

To obtain some idea of what radiotherapy alone has managed to effect in our advanced cases, I have analysed all those cases that should have undergone laryngectomy, if they had not received irradiation. I have also gone through the results of irradiation alone in all cases with fixed vocal cord.

In 46 cases the tumour was so widespread that the only possible surgical procedure would have been laryngectomy. In 10 of these cases the laryngologist decided not to operate owing to the patient's age or poor general condition, and in another 4 cases the patient refused to undergo laryngectomy. In the other cases relatively young people were concerned; irradiation was considered worth trying and if unsuccessful could be followed by operation. *In 18 of the 46 cases a five-year cure was obtained exclusively by irradiation.* In another 4 cases a five-year cure was obtained but the cases had recurrences which demanded a secondary laryngectomy. Ten cases died from reactions or from intercurrent disease; the former were old and in poor general condition; sections of the involved area showed no sign of any growth.

Baclesse (1949) treated 238 cases which otherwise would have had to be subjected to laryngectomy with radiotherapy and obtained a 15 % five-year cure.

In 32 of our cases that were only irradiated, the vocal cord was entirely fixed. In 25 of these cases the tumour had grown through the larynx and had infiltrated the surrounding tissues. In 5 cases a five-year cure was obtained. Another 4 patients died from intercurrent disease. Autopsy was performed in all these cases.

The following are abbreviated records of each of the five-year cures with a fixed vocal cord, treated with irradiation alone.

Case 1. Record No. 8251/39. A. C., labourer, aged 58. Ulcerated tumour extending over the greater part of the right half of the larynx and sinus piriformis. Right half of the larynx fixed. Biopsy, papillomatous squamous carcinoma. L. gl. metastasis, 2.5 × 2 cm, below the middle of the right sternocleidomastoid. Teleradium treatment of primary tumour and metastasis. At control examination three months later, free from signs of both primary and secondary growth. For last twelve years, free from trouble and fully fit for work.

Case 2. Record No. 1701/42. E. E., schoolmistress, aged 58. For five years treated by laryngologist for hoarseness; had not been able to work as teacher for previous four years; vocal cords had been red and swollen; increasing hoarseness during previous two months; had severe stridor necessitating tracheotomy before treatment. Tumour proliferation on left false cord with oedema and redness of left side of larynx which was fixed. Biopsy, solid, low-differentiated carcinoma. No l. gl. metastases. Teleradium treatment to each right and left lateral field. Complementary roentgen therapy as the radium treat-

ment could not be administered anteriorly in the usual manner owing to a cannula in situ. Cured for nine years.

Case 3. Record No. 9588/44 H. A. Consul, aged 63. Hoarse for two months. Ulcering, infiltrating tumour of left vocal cord, anterior commissure and anterior part of right vocal cord. Left half of larynx fixed. No lymph gland metastases. Biopsy, squamous cell carcinoma with trace of keratinisation. Teleradium treatment over 14 days. Free from signs after one month, then for more than five years and died from an intercurrent disease.

Case 4. Record No. 5972/44. M. W., woman, aged 40 with rapidly increasing hoarseness and stridor. Tracheotomy previous to treatment. Tumour involving right vocal cord, sinus Morgagni and epiglottic region. Both vocal cords fixed. Biopsy, papillomatous squamous cell carcinoma with some keratinisation. No lymph gland metastases. Teleradium treatment over a period of 15 days. Two months later, moderate oedema of the larynx but no growth; seven years later, alive and well and free from symptoms.

Case 5. Record No. 16063/45. T. J., warehouseman, aged 58; hoarseness, one year. The greater part of the left vocal cord, left false cord, anterior commissure and anterior part of the right vocal cord infiltrated by nodular growth. Left half of larynx fixed. Biopsy, squamous cell carcinoma. No lymph gland metastases. Teleradium treatment over a period of 13 days. Cured after 2 months; alive and free from symptoms 6 years later.

At this stage, the results in those cases with a fixed vocal cord or fixed half of the larynx primarily operated on and post-operatively irradiated, should be mentioned. In 31 cases laryngectomy was performed and post-operative irradiation given; of these, 22 became five-year cures and another 3 were cured but died from intercurrent disease.

Infiltration of the ary-region in cancer of the vocal cord is regarded as prognostically unfavourable. LENZ considers that »the gravity of invasion of the arytenoid cartilage in the treatment of cancer of the larynx by roentgen cannot be exaggerated». In 68 cases where the vocal cord was fixed owing to invasion of the ary-region, he obtained a five-year cure of 12 % of cases treated by roentgen therapy.

In our material there are 3 cases of cancer of the vocal cord with invasion of the tumour only into the ary-region. All three cases were treated by teleradium alone and became five-year cures.

In 1931 another patient was treated at Radiumhemmet by teleradium alone for a cancer that occupied the posterior part of the right vocal cord with infiltration of the false cord and the ary-region. The tumour was ulcerated and infiltrating and the right half of the larynx was fixed. Teleradium treatment was given. The patient is alive and free from symptoms after treatment 20 years ago.

B. Site of primary tumour.

ACKERMAN and REGATO, BACLESSE, CUNNING, ZANGE and others advise laryngectomy in those cases in which the tumour is growing down

into the subglottis and the rare cases of pure tumours of the subglottis. Cancer of the subglottis often grows submucosally and infiltrates the cricoid cartilage at an early stage.

BACLESSE (1949) treated 10 cases of cancer of the subglottis by roentgen and obtained a cure in only one case. NIELSEN (1950) has also reported only one case cured out of 10 treated.

In our material there were 5 cases of cancer of the subglottis. In three cases laryngectomy was performed and post-operative irradiation given; cure was obtained in only one of the cases, the patient being alive and free from symptoms 7 years later. In two cases teleradium treatment alone was given and cure was obtained in one; in this case — free from symptoms for 6 years — there were large bilateral lymph gland metastases which on one side were fixed.

Tumours of the false cords and of the epiglottis are generally considered radio-sensitive (CUTLER, LENZ and others). LENZ had 9 five-year cures in 28 cases of carcinoma of the epiglottis treated by roentgen, and NIELSEN had 4 cures in 8 cases treated. NIELSEN also had 3 cures in 11 cases of cancer of the false cord treated by roentgen therapy.

In our material there were 7 cases of cancer of the epiglottis. Of these, two became five-year cures; one following laryngectomy, removal of the lymph gland metastases and post-operative teleradium treatment, the other following teleradium treatment only. This latter patient was 72 years old at the time of treatment and nine years later is alive and free from symptoms. The other 5 cases were advanced, inoperable cases and received irradiation only.

In 4 cases the laryngologist stated that the tumour had arisen from the false cord. In two of these, treated by laryngectomy and post-operative teleradium, five-year cures were obtained. In two cases, both advanced and inoperable, only teleradium treatment was given. None of these cases was cured.

C. Lymph node metastases.

The existence of metastases of the lymph glands in cancer of the larynx makes the prognosis very considerably worse. BACLESSE (1950) treated 49 cases with metastases with roentgen and obtained a five-year cure in two cases. TOD and PATERSON (1950) treated 24 cases with metastases of the lymph glands likewise, and obtained a five-year survival in 8 % of the cases.

Operable metastases of the lymph glands in laryngeal cancer are generally treated only by neck-dissection or combined with radiotherapy. MARTIN (1947) performed neck dissection in 12 cases and obtained five-year cures in 4.

In our material there were metastases of the lymph glands in 37 cases. 8 cases were operated on and postoperatively irradiated; in 3 of these cases five-year cures were obtained. The other cases were treated only radiologically and 2 became five-years cures. Altogether 5 out of 37 cases of metastases of the lymph glands in our material were thus five-year cures.

Both the primary tumour and the metastases were inoperable in half of the cases in which the metastases were irradiated only and in the others, either the metastases or the primary tumour were inoperable.

D. Microscopical structure.

The prognosis in the case of highly differentiated squamous-celled carcinomata is usually better than in the case of low-differentiated types and the laryngeal carcinomata form no exception in this respect.

The difference in prognosis depends mainly on the fact that low-differentiated laryngeal cancers are advanced and metastasized to a considerably greater extent by the time they arrive for treatment than the highly differentiated growths.

In our material there were 15 cases of low-differentiated squamous-celled carcinoma and all these cases belonged to Group IV. In $^2/_3$ of the cases there were metastases of the lymph glands. In most of these cases the tumour was so extensive that it was impossible to be sure of its starting point. In 8 cases the tumour was irradiated only and in one of these a five-year cure was obtained. In the other 7 cases laryngectomy and post-operative teleradium treatment were the procedures of election; in 3 of these five-year cures were obtained.

Failure of Radiotherapy in Operable Cases

In this present material radiotherapy has been carried out in 8 operable cases which, owing to subsequent recurrences, had to be operated on secondarily. One of these cases belonged to Group I and the tumour recurred $1\,^1/_2$ years after the teleradium treatment; the secondary operation was successful; the patient died later from intercurrent disease. In 4 cases the tumour belonged to Group III and in one of these cases recurrence appeared as late as 4 years after treatment. In 3 of the cases the patient became free from symptoms after the secondary operation and a five-year cure was obtained. In the fourth case however, the tumour had become too advanced and operation was not sufficiently radical. In 3 cases the tumour belonged to Group IV; only in one of these could the tumour be radically removed by secondary operation and a five-year cure effected. There is thus a risk that an originally operable tumour may, during or after irradiation, become inoperable.

Radiotherapy, as given at Radiumhemmet, has not, however, seemed to aggravate a later operation or involve the risk of necrosis after such operation.

In one of the above-mentioned cases the only possible surgical procedure on admission would have been laryngectomy. After irradiation the tumour disappeared but a recurrence appeared 8 months later. Laryngo-fissure and cordectomy now proved sufficient. The record of this case was as follows: *Case N. D.* Record No. 4084/43. Farmer, aged 57; hoarseness 1 year. Right vocal cord, sinus Morgagni and false cord involved by a nodose tumour. Good mobility of vocal cord. Biopsy, papillomatous squamous-cell carcinoma with some keratinisation. No lymph gland metastases. Laryngologist considered that operative procedure ought to be laryngectomy. Teleradium treatment of 5,000 r on each side field and 4,500 r on a centre field was given. The treatment was carried out over 13 days and the tumour-dose was 6,200 r. The patient was free from symptoms 3 months later. There was a recurrence on the vocal cord after a further 5 months. Laryngo-fissure and cordectomy was performed. Cure without incident in spite of the heavy irradiation. The patient has been free from symptoms for 8 years.

A Second Primary Cancer

In a large cancer material a second primary cancer appears up into 7 % of the cases (Engelbreth-Holm, Warren and Gates, Weyde).

In women suffering from sideropenia with tongue or hypopharyngeal cancer a second primary cancer is encountered to a greater extent than in the average cancer patients (Ahlbom, Jacobsson).

In our material of laryngeal cancer 7 % of the patients had a second primary cancer. No predilection for the digestive tract as in the case of cancer associated with sideropenia, occurred.

Complications

Perichondritis is the most important and difficult complication in the treatment of carcinoma of the larynx. From the literature however, it is hard to obtain information about how often it occurs. It may also not be easy to decide in some cases whether perichondritis starts in association with infection in a tumour growing in the cartilage, or as a consequence of radiotherapy or both.

The cartilages of the larynx gradually become calcified and, in old men, are often partially ossified. During radiotherapy of laryngeal carcinoma, the cartilages are situated in the path of the rays and receive a considerable dose. To avoid necrosis of cartilage one has, in several cases, excised the thyroid cartilage before treatment.

COUTARD obtained cartilage necrosis in 60 % of those cases treated by roentgen at the Fondation Curie (cit. Baclesse 1949). BACLESSE (1949) on account of this experience has given the treatment over a considerably longer period than Coutard. BACLESSE had cartilage necrosis after treatment in 7 ½ % of cases.

In our material, in spite of the intensive and concentrated treatment, perichondritis in connection with or after radiotherapy was encountered in only 7 cases (6 %) of the cases which received only irradiation.

Maybe these results were partly due to the fact that the absorption in cartilage and in calcified and ossified tissues is considerably lower in the case of the hard gamma-radiation with an energy of 1.5 million volts emitted by teleradium compared with the usual 200 kv roentgen radiation (SPIERS).

We are now able to treat acute laryngeal oedema in a much better way than before. Previously it was nearly always necessary to perform tracheotomy with subsequent risk of necrosis of the cartilage. Penicillin is now given and the laryngeal oedema treated by media producing detumescence; these usually cause reduction of the swelling without the need for tracheotomy. By this as well as by improvements in technique gained from experience, we hope to be able still further to diminish the risk of complications from teleradium treatment.

Conclusions

In a material of 178 cases of laryngeal cancer, from 1935 to 1945, all were treated by radiotherapy. In some of the cases operation was performed primarily and irradiation given post-operatively. The composition of the material has made it possible to obtain a fairly good idea of the prognosis in laryngeal cancer as a whole.

In all the cases treated a net five-year cure rate of 57 % was obtained.

The material has been divided into four groups covering the situation and extension of the tumours.

In the cases irradiated only, including all the inoperable cases, a net five-year cure rate of 44 % was obtained.

In cases of cancer of the vocal cord with full or slightly restricted mobility of the cord (Groups I and II), teleradium treatment is the method of choice and has given primary freedom from symptoms in all cases in our material and permanent cure in most cases.

In cases of cancer of the vocal cord infiltrating surrounding tissues and with tumours in other parts of the larynx the prognosis is usually worse. This is partly due to the fact that there are metastases in many of these cases. The further from the glottis the tumour is growing the earlier and easier will metastases form. In carcinoma of the vocal cord

without infiltration there are however, practically no metastases. Lymph node metastases in such cases have not been noticed in this present material.

If a carcinoma of the larynx infiltrates cartilage, especially if the infiltration be so marked that there is gross oedema with or without fixation of half of the larynx, it is usually not advisable to employ radiotherapy alone.

It is necessary to be especially careful as regards the indications for primary therapy when the patients concerned are under 60 years of age and in good general condition. There is a risk that a tumour originally operable may, during or following irradiation, become inoperable. On the other hand, patients over 60 years of age have difficulty in learning oesophageal speech after laryngectomy and often become very depressed. Test radiotherapy is permissible in these cases if its risks be clearly explained to the patient.

By employing radiotherapy alone 18 patients have been spared laryngectomy. Two of these were only 23 years old and one 31 years old. Moreover, 5 cases that were inoperable had their lives saved by radiotherapy.

In spite of the concentrated and intensive teleradium treatment we have had few complications. This may to a certain extent be explained by the fact that absorption by the cartilage of the larynx is considerably less in the case of the hard gamma-rays of teleradium with an energy of 1.5 million volts compared with ordinary 200 kv roentgen radiation.

By continued experience gained from treatment of cases in which, from the extension of the tumour, operation is thought to be indicated but in which the patient is inoperable owing to »age, health or prejudice», we hope to be able to extend the indications for irradiation in laryngeal cancer. In this manner, more patients may be spared laryngectomy.

SUMMARY

The paper forms an analysis of a material of 178 cases of laryngeal cancer from 1935 to 1945. All the cases were either irradiated alone or in combination with operation. As a rule teleradium treatment was used. In the whole series of cases a net five-year cure rate of 57 per cent was obtained and in those only irradiated a rate of 44 per cent. The indications for radiotherapy in carcinoma of the larynx are discussed.

ZUSAMMENFASSUNG

Ein Material von 178 Fällen von Karzinoma laryngis aus den Jahren 1935—1945 wird analysiert. Alle Fälle wurden entweder ausschliesslich radiologisch behandelt oder kombiniert mit Operation. In der Regel wurde Teleradiumbehandlung gegeben. Es wurde eine 5-Jahresheilung von 57 % sämtlicher Fälle erzielt; in den nur mit Strahlen behandelten Fällen betrug sie 44 %. Die Indikationen für die Strahlentherapie des Larynxkrebses werden diskutiert.

RÉSUMÉ

Analyse de 178 cas de cancer du larynx de 1935 à 1945. Tous ces cas ont été irradiés, avec ou sans opération associée. En règle générale la télecuriethérapie fut employée. Dans l'ensemble de la série on a obtenu 57 % de guérisons de 5 ans, et 44 % dans ceux qui ont été seulement irradiés. L'auteur discute les indications de la radiothérapie dans le cancer du larynx.

REFERENCES

Ackerman, L. V. and Regato, J. A.: Cancer, diagnosis, treatment, prognosis. St. Louis 1947.

Ahlbom, H. E.: Die Resultate der Strahlenbehandlung von endolaryngealen Karzinomen am Radiumhemmet, Stockholm, von 1930 bis 1939. Acta Radiol. 22 (1941), 539.

— Beitrag zur Kenntnis der multiplen Plattenepithelkarzinome der Schleimhäute. Radiološki Glasnik 2 (1938), Broj. 1—2.

Baclesse, F.: Carcinoma of the larynx. Brit. J. Radiol. Suppl. No. 3, 1949.

— Roentgentherapy of cancer of the larynx. Abstracts of papers, Sixth international congress of radiology, London, 1950.

Cade, S.: Malignant disease and its treatment by radium. Vol. II, Simpkin Marshall Ltd., London, 1949.

Coutard, H.: Roentgen therapy of epitheliomas of the tonsillar region, hypopharynx and larynx from 1920 to 1926. Am. J. Roentgenol. 28 (1932), 313.

— Present conception of the treatment of cancer of the larynx. Radiology 34 (1940), 136.

Cunning, D. S.: Choice of treatment in cancer of the larynx year 1949. Ann. Otol. Rhinol. & Laryngol. 59 (1950), 467.

Cutler, M.: Cancer of the larynx. Arch. Otolaryng. 43 (1946), 315.

— Radiotherapy of early cancer of the larynx. J. A. M. A. 142 (1950), 957.

Engelbreth-Holm, J.: Om multiple carcinomer i mund-svælg-oesophagus. (Danish. English summary.) Nord. Med. 16 (1942), 3171.

Frenckner, P.: Some primary results in operative treatment of cancer of the larynx. Acta oto-laryngol. 21 (1935), 539.

Jackson, Chevalier and Jackson, C. L.: Cancer of the larynx. W. B. Saunders Co., Philadelphia 1939.

Jackson, C. L. and Blady, J. V.: Criteria for the selection of treatment of cancer of the larynx. Arch. Otolaryngol. 37 (1943), 672.

Jacobsson, F.: Carcinoma of the tongue. Acta radiol. Suppl. 68, 1948.

— Carcinoma of the hypopharynx. A clinical study of 322 cases, treated at Radiumhemmet from 1939 to 1947. Acta radiol. 35 (1951), 1.

Lederman, M.: Cit. Cade.

Lenz, M.: Roentgen therapy in cancer of the larynx. J. A. M. A. 134 (1947), 117.

Low-Beer, B. V. A.: Radiation therapy of cancer of the larynx. Laryngoscope 60 (1950), 696.

Martin, H.: Cancer of the larynx. Nelson's Loose Leaf Surgery. Nose and Throat Vol. 1947.

Mustakallio, S.: Über das Larynx- und Hypopharynxkarzinom, ihre Röntgenbehandlung und die Ergebnisse der Therapie. Acta radiol. 25 (1944), 13.

— Relation of microscopic structure of laryngeal cancer to radiocurability. Acta radiol. 27 (1946), 473.

New, G. B., Figi, F. A., Havens, F. Z. and Erich, J. B.: Carcinoma of the larynx. Surg. Gynec. & Obst. 85 (1947), 623.

Nielsen, J.: Function and permanence of results in roentgen therapy of intralaryngeal carcinomas. Abstracts of papers, Sixth international congress of radiology, London 1950.

Oeser, H.: Die Strahlenbehandlung des endolaryngealen Karzinoms. Strahlentherapie 73 (1943), 361.

— Die Strahlentherapie der bösartigen Geschwülste des Kehlkopfes und Kehlkopfrachens. Arch. Ohr. usw. Heilk. u. Z. Hals, usw. Heilk. 159 (1951), 59.

Paterson, R.: Discussion on the technique of radiotherapy in pharyngeal and laryngeal cancer. Proc. R. Soc. Med. 36 (1943), 267.

Paterson, R., Tod, M. and Russell, M.: The results of radium and X-ray therapy in malignant disease. E. & S. Livingstone Ltd., Edinburgh 1950.

Sievert, R.: The new apparatus for teleradium treatment used at Radiumhemmet. Acta radiol. 14 (1933), 197.

Spiers, F. W.: Effective atomic number and energy absorption in tissues. Brit. J. Radiol. 19 (1946), 52.

— The influence of energy absorption and electron range on dosage in irradiated bone. Brit. J. Radiol. 22 (1949), 521.

Taylor, G. W. and Nathanson, I. Th.: Lymph node metastases. Oxford University Press, New York 1942.

Warren, S. and Gates, O.: Multiple Primary Malignant Tumours. Am. J. Cancer 16 (1932), 1358.

Weyde, R.: Plummer-Vinson Syndromet. Sideropeni-anemien og Plate-epitelcarcinomene i Munnhule-Svelg-Spiserör hos Kvinner. (Norwegian.) Tidsskr. f. d. Norske Lægefor. 67 (1947), 194.

Willis, R. A.: Pathology of Tumours. Butterworth & Co., Ltd., London 1948.

Windeyer, B. W.: Intrinsic Carcinoma of the Larynx. Proc. R. Soc. Med. 40 (1947), 522.

Zange, J.: Chirurgie und Strahlentherapie der bösartigen Geschwülste des Kehlkopfes und Kehlkopfrachens. Arch. Ohr. usw. Heilk. u. Z. Hals usw. Heilk. 159 (1951), 1.

BOOK REVIEWS

CARCINOMA OF THE UTERINE CERVIX. INCIDENCE AND INFLUENCE OF AGE. A STATISTICAL STUDY. By ARNE LINDELL. 102 pp. 18 diagrams and 38 tables. Acta radiol. Suppl. 92. Stockholm 1952. Swed. Kr. 20: —.

The investigation deals with two problems concerning carcinoma of the uterine cervix: (1) the influence of age on the prognosis and on various other factors, and (2) the morbidity rate in various ages and during different periods of time.

The material in the first part consists of 5,258 cases of cervical carcinoma treated at Radiumhemmet, Stockholm, during the period, 1914 to 1944. The material is representative, carefully recorded and followed-up.

The annual number of cases grew considerably during the 31 years covered by the investigation. The distribution among the different stages varied widely. Stage II showed a considerable relative increase at the expense of Stages III and IV, but Stage I on the whole remained unchanged.

The age distribution corresponds well with that observed by other authors. The mean age decreased during the period from 50 to 49 and finally to 48 years.

Young women were more often found in the early stages, while older women more frequently belonged to the advanced stages. Of the women under 31 years, 32 per cent were in Stage III or IV, while the corresponding figure for those over 45 years was 56 per cent.

Intercurrent deaths are discussed as well as different methods of correcting the errors in the therapeutic results that arise if the intercurrent deaths are included as cancer deaths.

The therapeutic results in various ages and during different periods of time are investigated. With regard to Radiumhemmet's material of cervical carcinoma, each stage was studied separately and the cases were assembled in ten-year age-groups and in two periods of time, 1914 to 1934 and 1935 to 1944. Correction for intercurrent deaths was made. Considerable differences were found between the results before and after this correction, particularly, as might be expected, in the upper age-groups. Only the corrected results are examined in any detail and statistically analyzed. The straight regression lines were calculated by the method of least squares. There was a trend toward better therapeutic results for older patients in all stages and periods. The only exception was Stage IV for the period 1935 to 1944. However, the results were very unstable in this group with only few cases apparently recovered.

In order to examine the stability of the upward trend, it was necessary to study the significance of the parameter values obtained. For this purpose the so-called *arc sin* transformation was used. The results secured indicate that the prognosis improves with increasing age, that this applies to all stages where the material is statistically reliable, but that there is not statistical significance in all groups.

The mortality rate during the first five years after treatment was studied. It varied in different ages. Most of the deaths occurred during the first two years. In the young

women the carcinoma ran a rapid course with most of the deaths during the first and second years. In the older ones, the course was slower, with the mortality rate divided more evenly among all five years.

The duration of symptoms was also investigated. It was found that the longer the duration of symptoms, the more advanced was the stage. In each separate stage, there was no definite correlation between the duration of symptoms and the prognosis. Only in cases of very slow progress with duration of symptoms of one year or more did the prognosis appear to be somewhat better. The duration of symptoms was generally longer in the older women.

The second part of the study is concerned with the incidence of cervical carcinoma in Sweden, the investigation covering practically all the cases (10,863) for the period 1920 to 1949. The morbidity rate is studied for various ages and different periods of time. The highest morbidity rate occurred betwen the ages of 51 and 55 years. This underwent a considerable and steady increase. In fact, it has almost doubled in the past 25 years. It is emphasized that this increase cannot be apparent only, but must be based on a true rise in incidence.

The future rate of cervical carcinoma in Sweden is also discussed. The increasingly aging population in itself will mean a relatively small increase in the number of cancer cases, even if the rate remains unchanged. However, it is very probable that the increase noted hitherto will continue.

Autoreview.

DIE GESUNDE UND KRANKE WIRBELSÄULE IN RÖNTGENBILD UND KLINIK. Zweite Auflage. Von Georg Schmorl und Herbert Junghanns. 284 Seiten, 399 Abb. Georg Thieme Verlag, Stuttgart 1951. DM 69: —.

This great standard work was published in 1932 under the title »Die gesunde und kranke Wirbelsäule im Röntgenbild». Anatomic conditions were differentiated with the utmost thoroughness and richness of detail and the development of the spine and the anatomic characteristics at different ages were exhaustively described. Moreover, the various pathologic changes which were observed and carefully studied in the collected material of some ten thousand vertebral columns were reported.

This gigantic production has laid an extremely solid foundation for clinical work and roentgen diagnosis especially has benefited from this fundamental information. Roentgen-anatomic studies have continually progressed and thanks to roentgen diagnosis all details of anatomic and pathologic conditions of the spine have become available for clinical application and therapeutic procedures placed upon a logical basis.

The results gained from roentgen-anatomic investigations have in a great measure been incorporated in the Second Edition of the book published by JUNGHANNS in August 1951. The roentgenologic literature in this sphere is thus well-represented and the bibliography comprehensive. This modernization of the work has been stressed by the authors by the inclusion of the word 'Klinik' in the title The book still retains its original character as a standard pathologic-anatomic production. The former illustrative matter again appears in its entirety and is extended and the roentgen-clinical aspects have been included as a supplement and do not encroache upon the previous contents.

An imposing standard work has still further increased in worth by this completion and become to an even greater extent an inestimable treasury of roentgen diagnosis. On one point modernization has unfortunately been overlooked: the characteristic changes in the sacro-iliac joints are not mentioned in the chapter on spondylarthritis ankylopoetica.

Folke Knutsson.

Über die röntgenologischen Darstellungsmöglichkeiten des weiblichen Genitalapparates mit Hilfe von Jodöl und Jodsol. Von J. Erbslöh. Georg Thieme Verlag, Stuttgart 1951. DM 16: 80.

Investigations into the physicochemical properties of *Jodsol* and a number of iodized oils are described in detail. As a result of these investigations the author recommends *Jodsol* for hysterosalpingography and *Immetal* for fetography.

Reproductions of fetograms and hysterograms are given in a clinical section. The quality of the radiograms and the physico-chemical properties of the contrast media are correlated. As far as the quality of the hysterograms is concerned, the reproductions do not, in the reviewer's opinion, confirm the author's claim that Jodsol is superior to the water-soluble contrast media now commonly used.

The quality of the fetograms is obviously high, but the use of the method should perhaps be postponed until definitely non-injurious media are available. The manuscript was prepared in 1943 but its publication postponed until 1951, by when water-soluble contrast media had a strong foot-hold. Even at the time of publication the book was therefore unfortunately not up to date.

Olof Norman.